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IMPORTANCE OF EXTRAPLEURAL PNEUMOTHORAX IN THE COLLAPSE THERAPY OF PULMONARY TUBERCULOSIS

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INTRODUCTION

EXTRAPLEURAL pneumothorax continues to be one of the most controversial subjects in the collapse therapy of pulmonary tuberculosis. Claims are contradictory and confusing, in spite of published reports covering thousands of operations.

Although the method was first tried by Tuffier[1] in 1891 for pulmonary hemorrhage, results in the first series of cases were disappointing because of the tendency of the lung to reexpand. Attempts to overcome this expansion led to various methods of plombage. The extrapleural space was at first filled with muscle, paraffin, and other foreign bodies. None of these methods proved satisfactory, and Zorini[2] (1933) advocated a return to simple apicolysis. It remained, however, for Graf[3] (1937) and Schmidt[4] (1937) to popularize this procedure. In 1940 Dolley[5] and his associates reviewed approximately 2,000 cases from twenty-seven clinics and concluded that extrapleural pneumothorax will be instrumental in obtaining approximately 63 per cent of sputum conversion.

In spite of these encouraging reports, the procedure soon fell into disrepute, particularly in this country, and was, to a large extent, abandoned because of the numerous complications encountered and the relatively few good late results. The consensus of the Association on Thoracic Surgery expressed at its annual meeting in 1948 as reported by Meade[6] before the National Tuberculosis Association meeting of the same year was to the effect that extrapleural pneumothorax followed by air or oil refills should be reserved for patients with bilateral disease and low respiratory reserve. In general, no great importance was attached to the operation. Strenuous efforts have been made recently to rekindle interest in the procedure by focusing

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attention on lucite balls,[7] fiber glass wool,[8] and plastic sponges,[9] with which to maintain the extrapleural collapse. Outside of this country, however, the operation has not been forgotten. In fact, it has been widely used.

Martin Seip[10] of Norway has recently published a 131-page study in which he deals with about 1,000 cases of pulmonary tuberculosis treated in the period from 1937 to 1947. It is largely devoted to a comparison of the merits of thoracoplasty and extrapleural pneumothorax. Dr. Seip writes: "We were, for a long while, of the opinion that thoracoplasty was a safer and better method than extrapleural pneumothorax, and reserved the extrapleural pneumothorax to cases in which thoracoplasty was contraindicated for some reason or other. Most surgeons seem to have a similar opinion today. But little by little we have changed our mind and begun to perform extrapleural pneumothorax to a larger extent in cases in which, in earlier years, we would have performed thoracoplasty. And, in the last years, since 1945, we have performed many more extrapleural pneumonolyses than thoracoplasties."

The work of Alarcon,[11] in Mexico, is well known, and his recent book on surgical extrapleural pneumothorax should go far toward returning this important surgical procedure to the place in the treatment of pulmonary tuberculosis that it deserves.

A wide divergence of opinion is thus evident, and the value of the operation remains far from settled. It is generally recognized that this divergence is in good part explained by the type of patient subjected to the operation, to details of operative technique and follow-up, and the relatively recent introduction of antibiotics. What is needed, therefore, is continued painstaking study and elucidation.

The likelihood in this country today is not so much that too many extrapleural pneumothorax operations will be performed or that they will be undertaken in an indiscriminate manner, but that the operation will be discarded or used only in exceptional cases.

CLINICAL MATERIAL

In the following pages a review is presented of 129 extrapleural pneumothorax operations in a consecutive series of 121 private patients (eight bilateral operations) under care for pulmonary tuberculosis for varying periods during the past twelve years, and upon whom the operation was performed for a variety of conditions. In brief, there were ninety-one successful operations (70.6 per cent), twenty-one unsuccessful (16.2 per cent), and seventeen operative deaths (13.2 per cent) (Table I). This is an encouraging record when one considers the type of case subjected to surgery and the handicaps under which the surgery was carried out, particularly during the early years when no antibiotics were available and contraindications had yet to be learned first-hand.

These patients are believed to represent a fair cross section of the type of tuberculous patient in whom extrapleural pneumothorax surgery has been used. Many stages and varieties of tuberculosis are represented, from acute fulminating or galloping consumption to chronic, progressive, bilateral disease with

TABLE I. RESULTS IN 129 CONSECUTIVE EXTRAPLEURAL OPERATIONS (8 BILATERALS) on 121 PATIENTS*

TYPE OF CASE	NO. OF OPERATIONS	OPERATIVE DEATHS	UNSUCCESSFUL OPERATIONS	SUCCESSFUL OPERATIONS
I. Exudative Tuberculosis (79 cases)				
A. Acute (18 cases)				
a. Pred. Unilateral (7 cases)	7	1	2	4
b. Bilateral (11 cases)	13 (2 bilateral)	2 (1 bilateral)	2 (1 bilateral)	9
B. Sub-acute (61 cases)				
a. Unilateral (14 cases)	14	0	3	11
b. Pred. Unilateral (18 cases)	18	0	3	15
c. Bilateral (29 cases)	32 (3 bilateral)	3	5 (1 bilateral)	24 (2 bilateral)
II. Fibro-ulcerative (42 cases)				
a. Pred. Unilateral (13 cases)	13	1	2	10
b. Bilateral (29 cases)	32 (3 bilateral)	10 (1 bilateral)	4 (1 bilateral)	18 (1 bilateral)
Totals	129	17 (13.2%)	21 (16.2%)	91 (70.6%)

*Many stages and varieties of tuberculosis are represented from the acute fulminating to the chronic bilateral, progressive with deteriorated general health. The late results clearly indicate that this single stage operation can be used successfully in patients not suitable for either thoracoplasty or resection.

deteriorated general health (Table I). All had either moderately or far-advanced disease at the time of surgery, and with few exceptions were not suitable for, or could not benefit from, other forms of collapse therapy. Pneumothorax was tried in all without success. In some, phrenic nerve interruption reinforced with pneumoperitoneum had also failed. In retrospect, perhaps twelve patients could be considered desirable risks for thoracoplasty. I know the great majority of these patients intimately and have kept accurate and detailed notes with repeated fluoroscopic, roentgenographic, and sputum studies. All patients in the series were adults; 119 whites, 2 Negroes; 68 were males, and 53 females. In fifty-two, the operation was performed on the left side, and in sixty-one, on the right. In eight, the operation was performed bilaterally.

The intelligence, cooperation, and morale of these patients were on a higher plane than one usually encounters in clinic patients. Furthermore, I not only carried out the initial surgery in the first place, but was also directly responsible for the follow-up treatment and the management of complications, on the principle that extrapleural pneumothorax is a one-man task. These points are worth stressing, for, by limiting the study to such a selected group, the results should represent the more favorable side of extrapleural pneumothorax and more than compensate for the relatively small number of operations reported as compared with other series in the literature.

CRITERIA FOR EVALUATION OF RESULTS

In evaluating the results of the operation, inherent difficulties arise which complicate a purely objective study. The value of the operation in each case

should, therefore, be appraised in a critical manner and on the basis of all associated factors. As already indicated, the great majority of patients whose postoperative course is made the basis of this study were making no noticeable progress at the time when extrapleural pneumothorax was undertaken. With few exceptions, they were confronted with progressive disease and uncertain, if not hopeless, outlook. Extrapleural pneumothorax appeared to offer the best, if not the only, chance for ultimate recovery.

It should also become clear that an impartial evaluation of the operation should be based primarily on the *changes that follow in the lung under consideration* and not necessarily upon the ultimate fate of the patient, unless, of course, the operation directly contributed to the downhill course of the patient. This suggestion is based upon the many clinical observations that the two lungs often behave differently in the same individual, and that the response of each to treatment will vary with the type and character of the collapse measure employed. Indeed, new infiltration or progressive and even fatal disease may be observed in the contralateral lung months and even years after the extrapleural pneumothorax. Or an intervening complication, such as tuberculous meningitis or contralateral spontaneous pneumothorax, may occur and kill the patient. Extrapleural pneumothorax may have nothing whatever to do with such developments.

The time element following operation is of extreme importance. There is general agreement that many of the immediate good results of extrapleural pneumothorax were later lost through new complications such as tuberculous empyema and obliteration of the space with reopening of the cavity. In speaking, therefore, of good results, one should keep in mind the time element following the surgery. The average period of observation of the 121 patients in this study was fifty-four months, with more than 50 per cent observed from three to eleven years, sufficient time to appraise late results and intervening complications.

Other factors to be considered in a fair appraisal of this operation are the inevitable modifications in operative technique and postoperative management which have been evolved by those who have persevered in the face of discouraging early results, modifications, and innovations which have materially altered the prognosis for the better. The relatively recent introduction of antibiotics is a major point in question. The full value of the operation should, therefore, be appraised in the light of these accumulated experiences and based on present-day technique and indications (Fig. 1).

In the interest of simplicity, the results of the operation are evaluated either as successful, unsuccessful, or operative death as of the time this report has been prepared (June, 1950).

By successful result is meant that all the objectives of the operation in the treated lung have been accomplished. This means that the diseased lung has been satisfactorily collapsed by the extrapleural pneumothorax and the collapse well maintained as of the time this report is prepared, that all cavities

are closed, and the disease in the lung well controlled as revealed by serial roentgenogram studies, including planigrams when indicated. It also implies that complications originally present have either disappeared or, if they still persist, are no longer troublesome and, in themselves, do not interfere with the well-being of the patient.

By the same token, unsatisfactory result does not necessarily imply that the patient received no important benefit from the operation. He might have had an excellent temporary result with cavity closure and negative sputum, only to have the cavity reopen in time and symptoms of toxemia reappear, even death supervene from progressive tuberculous disease. However, at the time of making this report, the early good result was lost and could not be re-established, so that the late result was unsatisfactory.

If agreement could be secured on such criteria as those indicated above, and the evaluation of extrapleural pneumothorax conducted within the limits implied, it would make possible an orderly appraisal of the operation, which should go far to eliminate the present confusion with its contradictory conclusions, by equally competent and sincere observers.

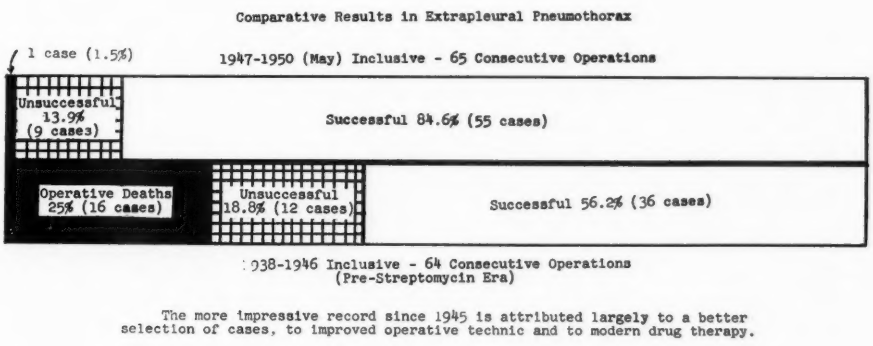
Comparative Results in Extrapleural Pneumothorax
1 case (1.5%)
1947-1950 (May) Inclusive - 65 Consecutive Operations
Unsuccessful 13.9% (9 cases)
Successful 84.6% (55 cases)
Operative Deaths 25% (16 cases)
Unsuccessful 18.8% (12 cases)
Successful 56.2% (36 cases)
1938-1946 Inclusive - 64 Consecutive Operations
(Pre-Streptomycin Era)
The more impressive record since 1945 is attributed largely to a better selection of cases, to improved operative technic and to modern drug therapy.

Fig. 1.

The cardinal questions to be answered, simply stated, are whether the extrapleural pneumothorax collapse was successful in controlling the tuberculosis in the *operated* lung, for how long, and at what risk. Furthermore, can the percentage of good results be increased materially in the future?

With the above considerations in mind, the evaluation of extrapleural pneumothorax will be presented under three main headings as follows: (1) the value of the operation as an independent collapse measure in selected cases, with a brief discussion of indications and contraindications; (2) analysis of unsuccessful operations and operative deaths encountered in this series and the lessons they teach; (3) suggested improvements in operative technique and follow-up which it is hoped will materially improve the percentage of good results in the future.

PART I

VALUE OF EXTRAPLEURAL PNEUMOTHORAX AS AN INDEPENDENT COLLAPSE MEASURE

One of the striking observations emerging from a study of the late results of the ninety-one successful operations (eighty-eight patients, three bilaterals) is the indispensability of this operation in any well-rounded collapse therapy program. In some patients with acute tuberculosis, it was dramatically life-saving; in others with chronic, but progressive, far-advanced bilateral tuberculosis, the operation was instrumental in bringing about a return to health and usefulness when other measures failed or could not be applied. In young women the operation proved more desirable than thoracoplasty. Then there were patients with uncontrolled pulmonary hemorrhage or pregnancy and active tuberculosis in whom the operation was a logical and happy solution. The operation was also of distinct value in elderly individuals and other substandard risk cases.

The value of the operation can, therefore, best be appraised in the light of the type of case subjected to surgery.

As has been indicated above, a detailed discussion of the various complications and operative deaths encountered in each of the groups of patients indicated below will be reserved for presentation at one time under Part II. For the present, emphasis will be placed on the positive achievements of this operation in the treated lung, with some indication of the risks involved.

Based on the clinical and roentgenologic appearance of the disease at the time of surgery, the patients in this series fall into three main groups: (1) patients with acute exudative tuberculosis; (2) patients with subacute exudative tuberculosis; and (3) patients with predominantly fibroulcerative but progressive tuberculosis. Each group in turn is subdivided according to the distribution of the disease into unilateral, predominantly unilateral, and frankly bilateral tuberculosis (Table I). Further subdivisions come to mind but are not desirable for the purpose of this study.

Patients with special problems at the time of surgery, such as serious pulmonary hemorrhage or pregnancy, are discussed separately from the particular view of the problem in question.

PATIENTS WITH ACUTE EXUDATIVE TUBERCULOSIS

Eighteen patients in this series had acute, caseating tuberculosis when first seen (Table I). In seven, the tuberculosis was predominantly unilateral; in eleven, it was advanced and active in both lungs with one lung more extensively involved. In addition, one patient had active intestinal tuberculosis and another active laryngeal tuberculosis. None of these patients were responding to bedrest. Pneumothorax was tried in each instance without success and had to be abandoned. Streptomycin, when it became available, was used without striking effect in six patients. Immediate thoracoplasty seemed too risky and, in retrospect, pneumonectomy almost certain death. The best that one could hope for was for the acute phase to burn itself out and for the disease to become

sufficiently stabilized in time to permit a reasonably safe attempt at thoracoplasty. For the most part, however, these patients were doomed unless immediate major collapse therapy could be resorted to promptly. It was under these unfavorable clinical conditions that extrapleural pneumothorax was undertaken to control the major area of disease.

Twenty extrapleurals were carried out on these eighteen patients. In two, the operation was performed bilaterally. Nine of the twenty operations, or 47 per cent, were carried out between 1938 and 1946 inclusive, before penicillin, streptomycin, and para-aminosalicylic acid became generally available, which are vital differences in the handling of such desperate cases. In spite of the pioneering nature of the operation and without the protective action of modern drug therapy prior to 1947, some of these desperately ill patients recovered and are alive today as a direct result of the extrapleural operation after everything else failed. In others, life was definitely prolonged, although the patient later died of progressive tuberculosis or some intervening complication not directly attributable to the operation, such as acute intestinal tuberculosis or laryngeal tuberculosis.

As stated under criteria for evaluation of results, basing the value of the operation in these acute cases on the result obtained in the lung collapsed by the extrapleural, the operation was completely successful in controlling the disease in the extrapleural lung in thirteen instances (65 per cent), unsuccessful in four (20.0 per cent), against an over-all operative mortality of three, or 15 per cent. This is a gratifying accomplishment. In fact, some of the most dramatic results in medical or surgical practice can be achieved with extrapleural pneumothorax in just such cases. The operation here is truly lifesaving, and is much less risky and much more effective than thoracoplasty or excisional surgery in controlling the major lesion. The following summarized histories illustrate this point.

CASE 1.—M. T., white woman, aged 20 years, first came under my care in January, 1941. She became ill only several weeks before while attending State Teachers College. Roentgenogram (Dec. 31, 1940) revealed advanced exudative tuberculosis with cavity (3 by 2 cm.) involving the right upper lobe. Sputum was positive for tubercle bacilli. Pneumothorax was established Jan. 6, 1941, but proved ineffective in spite of a pneumonolysis, and was discontinued and the lung reexpanded, all within six weeks. In the meantime, however, the cavity increased from 3 by 2 cm. to 4.5 by 5 cm., and the patient was worse clinically. Also flocculent disease made its appearance in the left lung at the level of the third anterior interspace (Fig. 2). On April 24, 1941, I performed an extrapleural pneumothorax on the right side. The cavity was closed shortly thereafter, and the sputum rendered negative, but there developed an acute mixed infection empyema of the extrapleural space which necessitated tube drainage for many months (to December, 1941). This was in the days before penicillin. The tuberculous flocculent disease in the left lung at the level of the third anterior interspace had also become more pronounced. In April, 1942, a small cavity was visualized in the left lung in the former area of flocculent disease, and an intrapleural pneumothorax was established on this side on April 29, 1942, with an immediate good result. On June 2, 1942, she married. In October, 1942, the right extrapleural pneumothorax was gradually converted into an oleothorax. On Jan. 22, 1943, she resumed her studies at Teachers College and in due course received a diploma. Shortly thereafter she started work as a teacher. During the war she travelled with her husband and received pneumothorax treatment in various Army hospitals (Fig. 3).

Fig. 2.

Fig. 3.

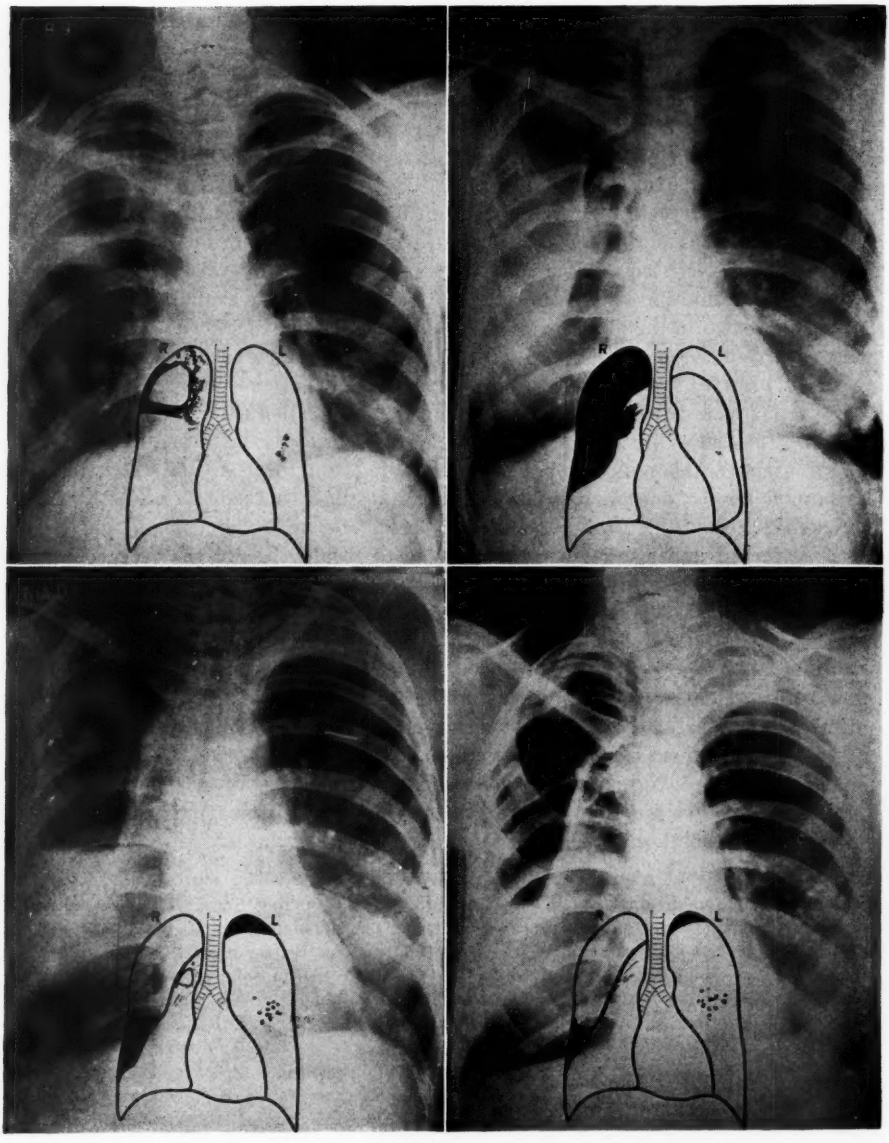

Fig. 4.

Fig. 5.

Fig. 2.—Case 1. M. T., female, aged 22 years, April 24, 1941. The cavity in the right upper has increased in size from 3 by 2 cm. to 4.5 by 5 cm. in the past six weeks. Also there is more disease in the left lower lung field. Pneumothorax right was unsuccessful. Patient accutely ill.

Fig. 3.—Case 1. Aug. 15, 1943. Patient well and working. Sputum negative. Right extrapleural (April 24, 1941) converted to oleothorax in October, 1942. New cavity in left lower lung field treated successfully with intrapleural pneumothorax (April, 1942). Note area of density in right lung at level of second anterior rib at the site of former large cavity.

Fig. 4.—Case 1. Dec. 6, 1946. Not doing well. Sputum again positive sixty-eight months after operation. During past six months fluid in right extrapleural space has increased underneath the oleothorax necessitating aspiration. Upon partial reexpansion a cavity appeared in former area of density at level of second anterior rib. Left pneumothorax discontinued as of April, 1946.

Fig. 5.—Case 1. April 17, 1950. Patient in excellent health, and physically active nine years after operation. Right extrapleural maintained. Small quantity of fluid present requiring aspiration from time to time.

On Feb. 3, 1946, she gave birth to a healthy male child without incident. Pneumothorax on the left side was discontinued shortly therafter due to an obliterating pleuritis. In November, 1946, the patient for the first time complained of feeling feverish (99.2° F.) and of increasing dyspnea. The area of density in the left extrapleural space was found definitely enlarged and 200 c.c. of thick, purulent fluid followed by 500 c.c. of mineral oil was aspirated from the right extrapleural space. It was decided to reexpand the right lung and obliterate the extrapleural space inasmuch as it was collapsed for more than five yers. A small cavity soon appeared in the right lung at the former site of cavity (Fig. 4), and the sputum again became positive on Dec. 7, 1946 (this was not believed to be a new cavity, but the remains of the old one which in reality had not been fully obliterated but had become filled and blocked off with inspissated retained secretions as witness the area of density at site of former cavity in Fig. 3). The collapse was promptly increased, the cavity closed, and the sputum rendered negative. It has continued negative since. At the present time there is a small collection of fluid in the right extrapleural space, at times turbid to purulent, but not toxic clinically, which requires aspiration from time to time (Fig. 5).

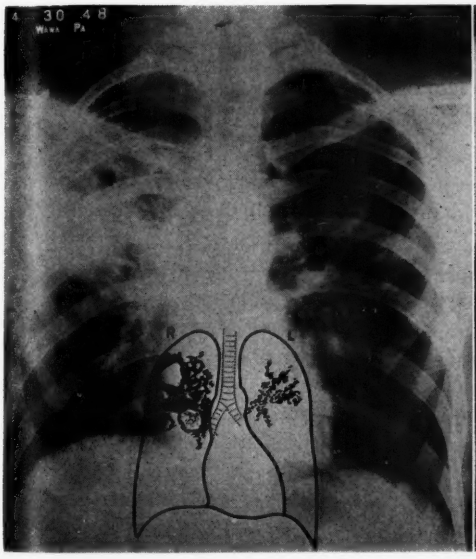

Fig. 6.

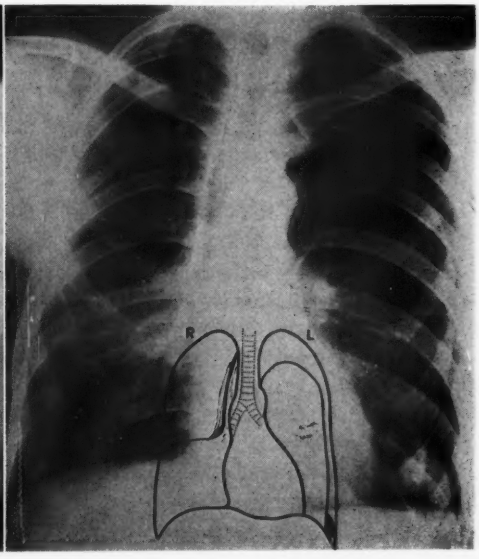

Fig. 7.

Fig. 6.—Case 2. J. F., male, aged 23 years. April 30, 1938. Acute disease and extensive cavity formation right upper, soft disease left upper. Pneumothorax right unsuccessful. Not responding to streptomycin. Acutely ill.

Fig. 7.—Case 2. May 17, 1950. Disease in right lung completely controlled with extrapleural pneumothorax (July 2, 1948), left with intrapleural pneumothorax (Sept., 1948). Patient in excellent health. Sputum negative.

This case recited in some detail illustrates the many pitfalls that can befall the extrapleural patient and how carefully he must be watched and handled over a period of years. It also brings into focus the indispensability of the extrapleural operation and its flexibility in permitting contralateral collapse. When the need for contralateral collapse arose in 1946, there was sufficient vital capacity and maneuverability to make it possible. The importance of extra-

pleural pneumothorax, therefore, in the long-range planning of therapy for the tuberculous patient can hardly be overestimated. Fortunately, the seriousness of mixed infection extrapleural empyema has been virtually eliminated with the aid of modern antibiotics as witness the following relatively recent case of acute tuberculosis treated successfully with extrapleural collapse.

CASE 2.—J. F., white male, aged 23 years, first came under my care in April, 1948, after an acute illness of several weeks. At that time he had far-advanced exudative tuberculosis involving the right upper lobe with one cavity 3 by 5 cm. just below the clavicle, and another large but poorly defined cavity in the apex of the lower lobe. Soft disease was also present in the left lung between the first and third anterior ribs (Fig. 6). The patient was placed on streptomycin therapy, and pneumothorax was established on the right side, but with indifferent success. In fact, clinically the patient was losing ground. Extrapleural pneumothorax was therefore performed on the right side on July 2, 1949, and approximately two months later a contralateral pneumothorax on the left side. The result to date has been excellent (Fig. 7). The sputum is repeatedly negative for tubercle bacilli, and the patient is free of symptoms. There has also been much resolution of the tuberculous disease originally present. No complications whatever followed the extrapleural surgery, and a dramatic result was achieved in the presence of otherwise hopeless tuberculosis.

PATIENTS WITH SUBACUTE, EXUDATIVE TUBERCULOSIS

Sixty-one patients in this series had advanced, progressive tuberculosis with little or no evidence of fibrosis in the roentgenogram when subjected to surgery (Table I). In fourteen, the disease was unilateral, in eighteen, predominantly unilateral, and in twenty-nine it was bilateral, with each lung extensively involved.

The disease, although for the most part exudative and progressive, was not acutely so, and symptoms of toxemia varied from mild to moderately severe. As was true with other groups in this series, these patients were not doing well at the time of surgery. Pneumothorax had been tried and found impractical. In one case phrenic nerve interruption also failed. With few exceptions, these patients were not considered good risks for thoracoplasty. Extrapleural pneumothorax, therefore, was resorted to in the belief that it was the best and quickest method of bringing the disease in the lung in question under control. Sixty-four extrapleural operations were performed on these sixty-one patients, three being subjected to bilateral operations.

Grouping the fourteen unilateral and eighteen predominantly unilateral cases together, the extrapleural accomplished the primary objective of bringing the disease in the tuberculous lung under control during the period of observation in twenty-six of the thirty-two patients subjected to surgery, or in 81.2 per cent. It was unsuccessful in six, or 18 per cent. There were no operative deaths.

In the twenty-nine patients with the disease extensive and advanced in the two lungs at the time of surgery, the operation was resorted to on the more diseased side. In three, however, it was performed bilaterally. The operation was successful in twenty-four of thirty-two operations (two bilateral), or 75.0 per cent, with three operative deaths, or 9.4 per cent. It was unsuccessful in five, or 15.6 per cent (one bilateral).

The following is a good example of what can be accomplished with bilateral extrapleural when faced with progressive exudative disease in both lungs and a poor prognosis.

CASE 3.—W. S., white man, aged 28 years, first came under my care on Feb. 7, 1949. Prior to that he was under treatment elsewhere for eighteen months. During that time, in addition to bedrest and sanatorium care, he had streptomycin therapy and pneumothorax on the left side. The latter was unsuccessful in closing the cavities, was complicated by a pleural effusion, and in time was abandoned. Pneumothorax was then attempted on the right side without success. Roentgenogram study, including planigrams, on March 1, 1949 (Figs. 8 and 9), revealed flocculent disease in the right upper lobe with a cavity 2 by 1 cm. in the outer zone of the second anterior interspace and three soft-walled cavities in the left upper seen best at a depth of 5 cm. from the posterior chest wall. The left costophrenic angle was obliterated and the pleura covered with considerable exudate. Clinically, the patient was underweight and in fair to poor health, with fever ranging from 99° to 100° F. Sputum was positive for tubercle bacilli. On May 6, 1949, I performed a left-side extrapleural pneumothorax and obtained an excellent result. In December, 1949, a new cavity appeared in the right lung at the level of the third right anterior rib. I, therefore, performed a right extrapleural pneumothorax on Jan. 20, 1950, and the cavity was promptly closed. The result to date has been more than gratifying. This patient is in good health. The sputum is negative for tubercle bacilli. In spite of the extensive bilateral extrapleural collapse (Fig. 10), he is ambulatory, and from the clinical standpoint has sufficient vital capacity for all ordinary needs.

What other surgical procedure could have accomplished so much, so easily?

PATIENTS WITH FIBROULCERATIVE, PROGRESSIVE TUBERCULOSIS

Forty-two patients in this series had advanced fibroulcerative tuberculosis with cavity formation and positive sputum. In thirteen, the disease was predominantly unilateral; in twenty-nine, it was bilateral and advanced in each lung; in two, there was a complicating intestinal tuberculosis; in one, severe laryngeal tuberculosis, and in another the tuberculosis was complicated with asthma.

All were definitely on the downgrade, clinically, with evidence of recent exacerbation of the tuberculosis. Pneumothorax and bedrest had been tried, but failed to bring the major area of disease under control. Phrenic nerve interruption was used in three patients, and phrenic nerve interruption reinforced with pneumoperitoneum in two others without lasting benefit. It is estimated that perhaps nine patients in the group with predominantly unilateral disease were suitable candidates for thoracoplasty, and very few, if any, in the bilateral group.

Forty-five operations were performed on these forty-two patients (three had the operation performed bilaterally).

Of the thirteen patients with predominantly unilateral disease, the extrapleural operation was successful in bringing the disease in the operated lung under control in ten (76.9 per cent). Two operations were unsuccessful (15.4 per cent). There was one immediate operative death (7.7 per cent), in the patient with asthma.

Thirty-two operations were performed on the twenty-nine patients with bilateral disease (three bilateral operations), the extrapleural was successful

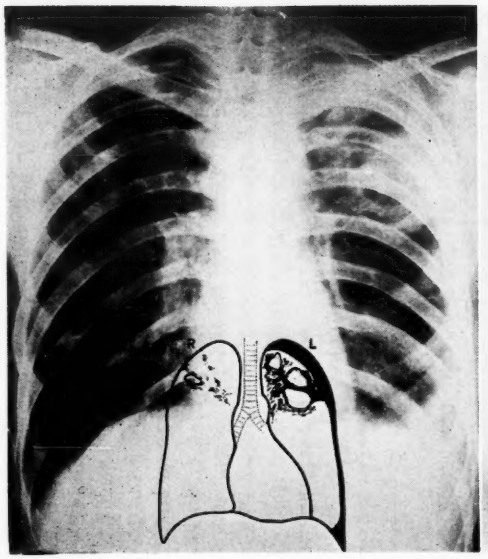

Fig. 8.

Fig. 9.

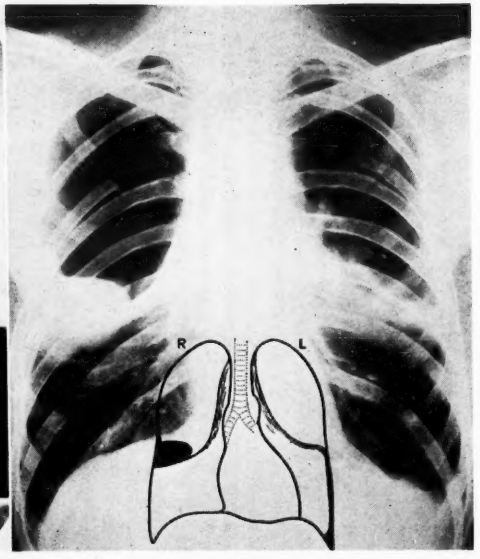

Fig. 10.

Fig. 8.—Case 3. W.S., male, aged 28 years. Mar. 1, 1949. Bilateral, progressive, subacute tuberculosis past eighteen months. Attempt at pneumothorax on each side, streptomycin and sanatorium care unsuccessful.

Fig. 9.—Case 3. Mar. 5, 1949. Laminograph of left lung at 5 cm. from posterior chest wall. Extensive cavity formation of left upper. No evidence of fibrosis.

Fig. 10.—Case 3. May 27, 1950. Bilateral extrapleural pneumothorax (left May 6, 1949, right Jan. 20, 1950 after new cavity appeared in upper lobe). Patient in excellent health, physically active, sputum negative.

eighteen times (one bilateral), or in 56.3 per cent, and unsuccessful four times, or 12.5 per cent. Operative mortality was high, ten deaths, or 31.2 per cent (one bilateral) largely because too many obviously doomed patients were included early in this series when enthusiasm was high and contraindications had to be learned first-hand. In fact, in five the cardiorespiratory reserve was so low and the general health so poor, that in retrospect they were beyond recovery, regardless of treatment, and in all probability would be denied surgery today.

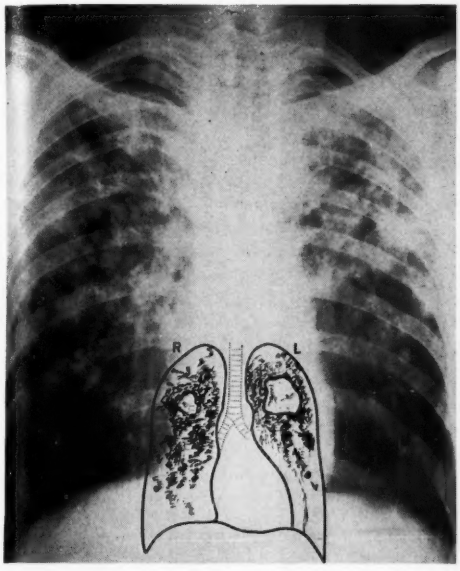

Fig. 11.

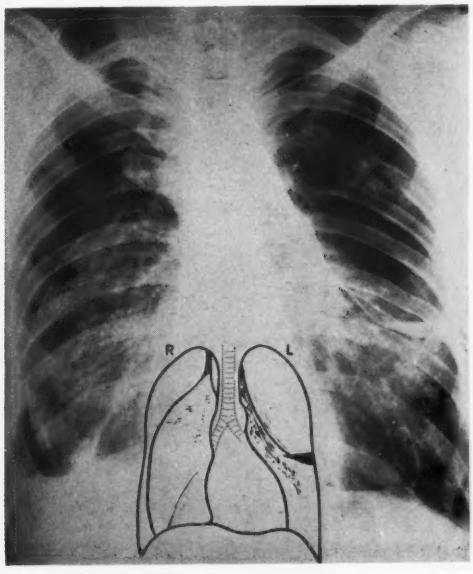

Fig. 12.

Fig. 11.—Case 4. F.U., male, aged 41 years. May 14, 1945. Extensive bilateral disease with cavity formation. Sputum positive. General health fair to poor. Ill one year. Pneumothorax left side unsuccessful.

Fig. 12.—Case 4. May 18, 1950. Patient in good health, working, sputum negative. Right side collapsed with intrapleural pneumothorax (July 1, 1945), left side with extrapleural, May 1, 1946.

In eighteen other patients in this group the disease was so extensive, so widely distributed in the two lungs, and the general condition of the patient was such as to make it technically impossible to bring all the disease under control by any single conventional method or combination of methods. Dolley and his associates, following the lead of Grof and Schmidt, consider such patients discouragingly unsatisfactory for extrapleural and classify them under "conditional" indications. Unfortunately, such patients constitute a considerable segment of our tuberculosis population and account, in large measure, for the high in-patient mortality reported in institutions throughout the country year in and year out.

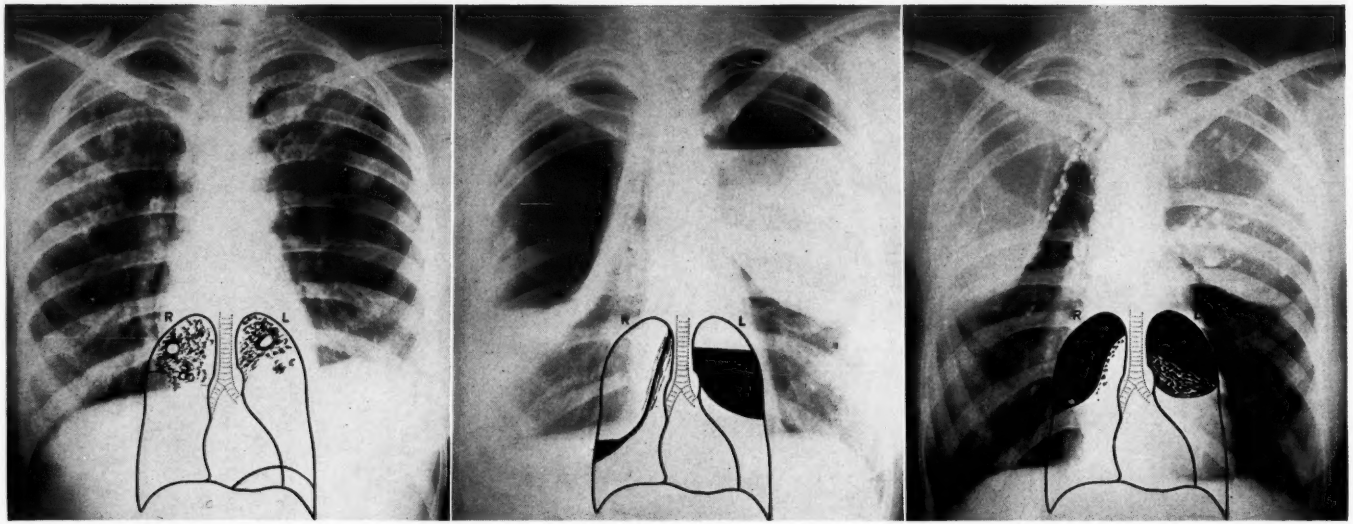

Fig. 13. Fig. 14. Fig. 15.

Fig. 13.—Case 5. H. C., female, aged 22 years. Mar. 2, 1939. Extensive bilateral fibroulcerative disease with cavity formation and positive sputum. Attempt at pneumothorax on each side, left phrenic interruption and bed rest unsuccessful.

Fig. 14.—Case 5. Nov. 20, 1940. Left extrapleural pneumothorax (Jan. 5, 1940), partially converted into oleothorax. Right extrapleural pneumothorax, Oct. 12, 1940. Patient in good health. Sputum negative.

Fig. 15.—Case 5. May 23, 1950. Excellent health. Physically active. Sputum negative. Upper lobes maintained in collapse with extrapleural oleothorax. No treatment since August, 1943.

The alternative to instituting extrapleural collapse in patients with far-advanced progressive bilateral disease, of course, is to let them die of tuberculosis. Yet many of these patients are still in fair physical condition and can tolerate one major surgical procedure. Success must be achieved with this one main effort or not at all. Under the circumstances, extrapleural pneumothorax is the procedure of choice for it is the only collapse measure which offers hope of ultimate recovery with a minimal decrease in pulmonary function.[12] In these patients it is in the nature of a salvage operation.

The ability to combine extrapleural pneumothorax with contralateral collapse and to perform bilateral extrapleural opens up many hitherto unexplored possibilities for recovery. If resorted to before the general health is not too badly deteriorated and the cardiorespiratory function not too seriously impaired by long-standing disease, many gratifying results will follow. The following cases are typical.

CASE 4.—F. U., white man, aged 41 years, was first seen May 14, 1945. Far-advanced bilateral fibroulcerative tuberculosis with multiple cavities and positive sputum (Fig. 11). Pneumothorax of the left side was unsuccessful. Pneumothorax on the right side established July 1, 1945, was successful, following pneumonolysis on Aug. 16, 1945. Continued bedrest and sanatorium care for one year resulted in only slight improvement of the disease in the left lung. The cavity remained open. Extrapleural pneumothorax on the left side was instituted on May 1, 1946. Excellent results have been recorded to date. Sputum negative. Patient working. Noticeable resolution of disease in both lungs (Fig. 12).

CASE 5.—H. M. C., aged 22 years, white woman. First came under my care on March 2, 1939, at which time she had far-advanced bilateral fibroulcerative tuberculosis with cavity formation in each lung and positive sputum. Pneumothorax was tried without success on each side. Sanatorium care and left phrenic nerve interruption had also failed (Fig. 13). Extrapleural pneumothorax was performed on the left side on Jan. 5, 1940, and converted to oleothorax three months later. This was followed by a right-sided extrapleural pneumothorax on Oct. 12, 1940 (Fig. 14), which was converted to an oleothorax in July, 1941. Bilateral extrapleural oleothorax has been maintained without incident and with no treatment whatever for the past nine years (Fig. 15). Sputum is persistently negative. Health is excellent. She lives a normal, active life with relatively few restrictions, is married, and has one child.

PATIENTS WITH SPECIAL PROBLEMS

A further critical review of the patients in this series brings to light particularly challenging problems present at the time of surgery, which were satisfactorily solved by the extrapleural collapse, and are deserving of special consideration. In the light of this experience, such problems when present should serve as added indications for the operation.

(a) *Young Women.*—Thirty-three patients in this series were under 25 years of age. Of this number, 20 were women. Young people, particularly unmarried women, dread the thought of thoracoplasty, with its telltale disfigurement and scar and aftermath of psychic trauma.

The gratifying clinical, psychological, and cosmetic results obtained with the extrapleural operation in this series cannot but impress one with the advantages of extrapleural over thoracoplasty in young people, particularly young women, even when there is a choice of therapy. Extrapleural avoids

extensive operations on the skeleton and well justifies the calculated risks and complications one is bound to encounter in this type of surgery. It does not set these young women apart, as does thoracoplasty, but enables them to lead more normal and happier lives. Cases 1 and 5 already cited can serve as examples. In addition, the following interesting case is presented:

CASE 6.—F. G. B., white young woman, was 16 years of age when she first came under my care in October, 1940. At that time she already had an advanced exudative type tuberculosis involving the left upper lobe with a cavity 2 by 2 cm. just below the clavicle. Sputum was positive for tubercle bacilli. Pneumothorax was instituted, a good result followed, and sputum became negative for tubercle bacilli. In August, 1941, new disease appeared in the right upper lobe in the outer zone of the first anterior interspace, which underwent early excavation. Sputum again became positive for tubercle bacilli. Pneumothorax was instituted on this side and the disease was promptly controlled. She continued with bilateral pneumothorax and enjoyed good health for the next four years. The right lung had virtually cleared. Treatment was therefore discontinued on this side as of November, 1945, and the right lung reexpanded. Within two months new disease appeared at the apex of the reexpanded lung, underwent early excavation (Fig. 16), and the sputum became positive. Pneumothorax could not be re-established. She was now 21 years of age. It was, therefore, decided to convert the left intrapleural pneumothorax into an intrapleural oleothorax and to collapse the right upper lobe extrapleurally.

I performed the extrapleural on Feb. 6, 1946, and after some difficulty because of a mobile upper mediastinum the cavity was closed and the sputum again rendered negative in July, 1946. The extrapleural space was also complicated by a severe tuberculous empyema (streptomycin was not available). The acute phase in time subsided, and although tuberculous fluid, at times purulent, but clinically nontoxic, has been present in the extrapleural space on and off, to this day she has remained in good health with negative sputum for the past four years. On Oct. 12, 1947, she married, and since then has given birth to a healthy male child. She does her own housework and lives a happy normal life.

Obviously this patient has intrinsic poor resistance to tuberculosis and the bilateral collapse has been maintained; the left with intrapleural oleothorax, the right with extrapleural pneumothorax (Fig. 17).

The latter was the ideal procedure with which to accomplish this fine result in spite of the troublesome complications encountered. Once she was freed of symptoms, her attitude toward life was wholesome and full of normal plans for the future, in contrast to what one often sees in young women with a successful but extensive thoracoplasty. This case also illustrates once more the absolute need for the extrapleural operation, in the collapse therapy program, despite anticipated troublesome aftercare.

(b) *Elderly Individuals.*—Elderly individuals, that is, patients in the fifth and sixth decades of life, with positive sputum and advanced disease, constitute a particularly important group of patients. If the disease cannot be brought under control and the sputum rendered negative by conventional methods, their problem becomes truly tragic, largely because of the social and public health problems involved. Very often such individuals live at home with their children and grandchildren and constitute a constant source of danger to their loved ones.

If an effective pneumothorax cannot be established, the majority are poor surgical risks for a major multiple-stage thoracoplasty, and one hesitates to advise it. On the other hand, many of these individuals are still in fair clin-

ical health and could tolerate one major operation, if not too shocking. The result must be accomplished with this one major effort, so to speak, or not at all. Under such circumstances, extrapleural pneumothorax is the only major collapse procedure which can be undertaken with reasonable expectation of rendering the sputum negative and restoring the individual to health and even earning capacity.

Eighteen patients in this series were more than 45 years of age at the time of surgery. Five of them were in their fifties, and two were 60 and 61 years of age, respectively. Extrapleural pneumothorax was well tolerated by this group. One patient, aged 47 years, went through a bilateral extrapleural without incident. There was no operative death. The following case is illustrative of what can be accomplished:

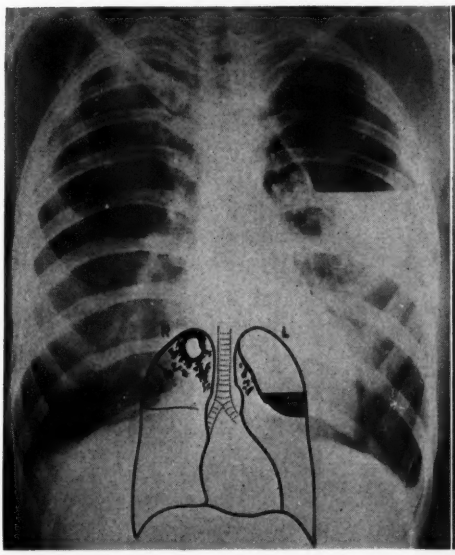

Fig. 16.

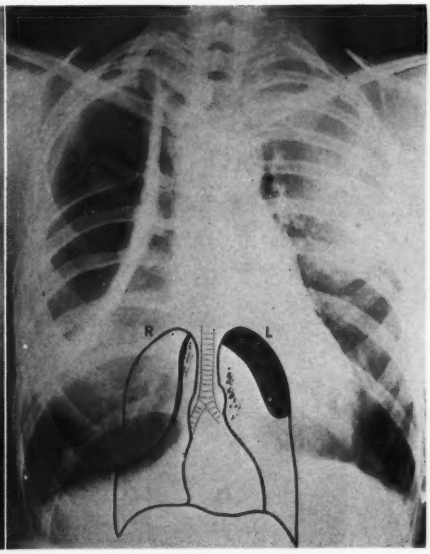

Fig. 17.

Fig. 16.—Case 6. F. G., female, 21 years of age. Jan. 10, 1946. Rapidly excavating tuberculosis at right apex in recently reexpanded lung (Nov. 18, 1945) following four years of successful intrapleural pneumothorax. Left lung maintained in good collapse with intrapleural pneumothorax, partially converted into an intrapleural oleothorax.

Fig. 17.—Case 6. May 27, 1950. Right extrapleural pneumothorax (Feb. 6, 1946), left intrapleural maintenance oleothorax since December, 1946. Sputum persistently negative. In excellent health. Physically active. Baby boy born on April 29, 1950.

CASE 7.—R. P., white male, 61 years of age, had advanced exudative type tuberculosis of the right upper lobe with a cavity 3 by 2.5 cm. in the region of the clavicle, when he first came under my care on July 8, 1947 (Fig. 18). Sputum was positive for tubercle bacilli. Pneumothorax was established, but the apex was found widely adherent and was therefore, discontinued within a month. In the meantime, the cavity had increased in size to 6 by 6 cm. (Fig. 19). I, therefore, performed an extrapleural pneumothorax on the right side on Sept. 5, 1947, and obtained excellent mobilization of the lung. The patient, however, had a troublesome cough, and the lung readhered to the chest wall two days later and could not be separated in spite of frequent high pressure refills. On Sept. 12, 1947, I

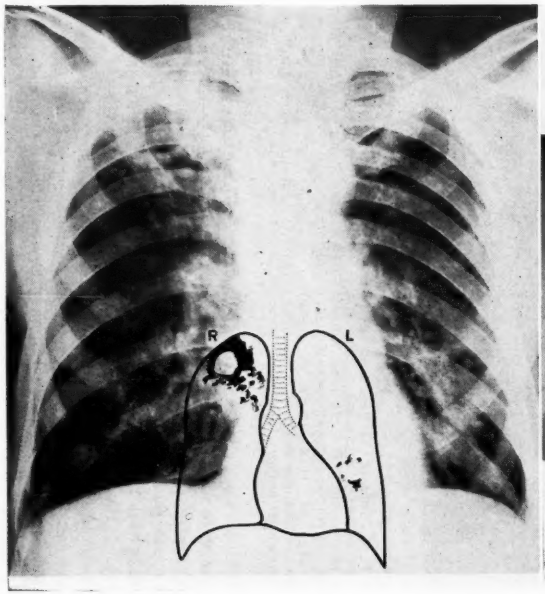

Fig. 18.

Fig. 19.

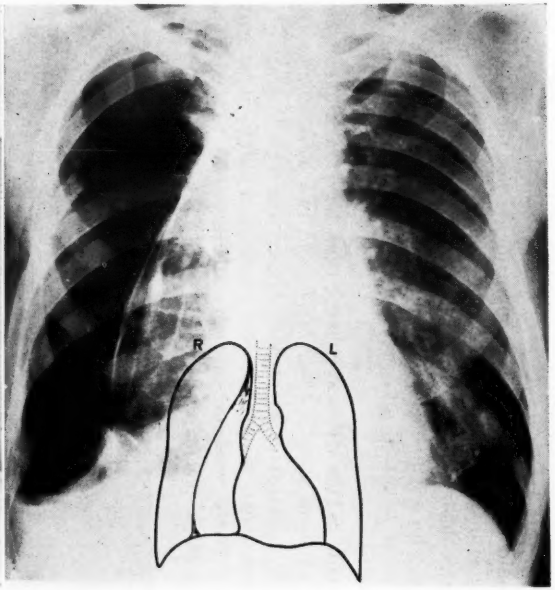

Fig. 20.

Fig. 18.—Case 7. R. P., male, 61 years of age. July 8, 1947. Progressive tuberculosis with cavity right apex, bronchogenic spread left lower. Pneumothorax unsuccessful. General condition fair.

Fig. 19.—Case 7. Aug. 21, 1947. Planigram of right upper. Cavity has increased from 3 by 2.5 cm. to 6 by 6 cm.

Fig. 20.—Case 7. Oct. 6, 1947. Cavity right apex closed following extrapleural, Sept. 5, 1947. Patient at present self-supporting, sputum negative (June, 1950).

reoperated and again mobilized the lung. It was relatively easy to do and well tolerated by the patient. The cavity promptly closed (Fig. 20). Some difficulty was later encountered with the wound and there is also a complicating tuberculous extrapleural empyema which requires aspiration from time to time. In spite of these difficulties, however, the cavity has remained closed and the sputum negative for tubercle bacilli since November, 1947. At present, the patient, at the age of 64, is self-supporting and enjoying a reasonably normal life.

(e) *Uncontrolled Hemoptysis.*—Serious pulmonary hemorrhage can well prove fatal in pulmonary tuberculosis. If it occurs in the presence of active, progressive disease which cannot be brought under control within a relatively short time, the prognosis is that much more serious, demanding heroic measures, even pneumonectomy. Extrapleural pneumothorax can be a dramatic and relatively safe way out of a difficult situation.

CASE 8.—G. H., a white young woman, 24 years of age, had advanced exudative tuberculosis, with cavity formation involving the left upper lobe and bronchogenic spread to the right upper lobe. This was complicated by serious and continued hemoptysis. Pneumothorax was tried on the left, but the collapse was ineffectual and had to be abandoned. The outlook appeared ominous. It was under such trying circumstances that a left-sided extrapleural pneumothorax was established on May 9, 1947, with complete success. This was a happy solution to what appeared to be a critical situation.

(d) *Open Tuberculosis and Pregnancy.*—On occasion one encounters a patient with open tuberculosis who is pregnant. If the sputum cannot be rendered negative with intrapleural pneumothorax, extrapleural offers a happy solution to an otherwise difficult and complicated problem.

CASE 10.—E. P., white woman, aged 31 years, presented the following problem on Nov. 8, 1945: she not only had moderately advanced fibroulcerative tuberculosis of the right upper with cavity formation and positive sputum and tuberculous deposits in the left lung in the region of the clavicle, but she was also two months' pregnant. The patient was anxious to have the baby and refused therapeutic abortion. Pneumothorax was attempted on the right, but there was no free space. A right-sided extrapleural pneumothorax was carried out on Dec. 6, 1945, with complete success. The sputum became negative shortly after the operation. On July 2, 1946, she gave birth to a baby boy. The extrapleural pneumothorax space has been converted into an oleothorax as of December, 1946, and has been maintained to this date without treatment except routine supervision.

She is enjoying excellent health, and her entire postoperative history, a matter now of four and a half years, has been entirely uneventful. No other surgical procedure could have done more for her.

(e) *Hilar Cavities.*—Patients with hilar cavities who have failed to respond to other collapse measures are a particularly important group for extrapleural pneumothorax. Located as these cavities are in the apex of the lower lobe and firmly adherent to the vertebral gutter, they are at times the most difficult of all cavities to close. When standard collapse measures fail, short of surgical removal, these patients are doomed. Extrapleural pneumothorax may bring about closure of such cavities and control of the disease at relatively little risk.

Four patients in this series had large hilar cavities as the dominant lesion. These cavities remained open in spite of prolonged bedrest, pneumo-

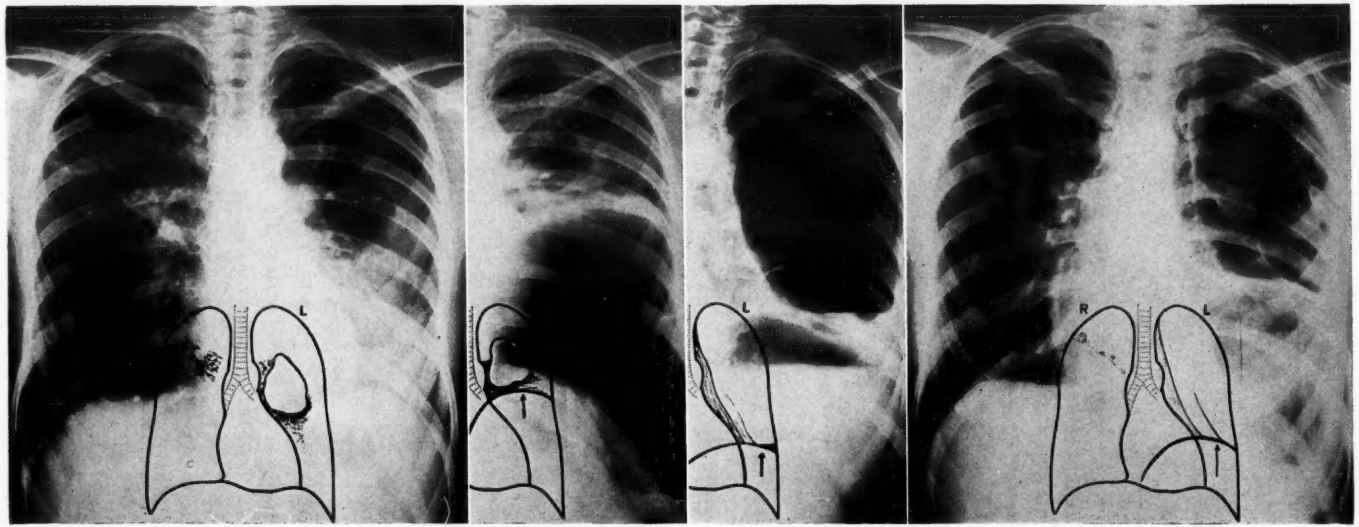

Fig. 21. Fig. 22. Fig. 23. Fig. 24.

Fig. 21.—Case 11. R. B., female, 24 years of age. April 27, 1945. Large hilar cavity in left lung, infiltration right upper.
Fig. 22.—Case 11. Jan. 5, 1946. Bed rest, left phrenic nerve interruption and pneumoperitoneum without favorable influence on large hilar cavity.
Fig. 23.—Case 11. Feb. 4, 1946. Excellent collapse of left lung with cavity closure following extrapleural, Jan. 22, 1946.
Fig. 24.—Case 11. May 4, 1950. Patient in excellent health. Working. Sputum negative. Partial reexpansion of left lung along anterior chest wall. Right lung improved.

thorax, and phrenic nerve interruption reinforced with pneumoperitoneum. Extrapleural was eminently successful in bringing about closure of the hilar cavities in two, and of distinct value in the other two.

The following summarized case report is illustrative of the ease and rapidity with which the desired result can at times be achieved.

CASE 11.—R. B., white woman, 24 years of age, has been ill with far-advanced tuberculosis since April, 1945. There was a large irregular cavity 6.5 by 4.5 cm. at the left hilum. In addition, there were moderately dense spots and fibrous strands in the right upper at the level of the second anterior interspace (Fig. 21). Sanatorium care, phrenic nerve interruption, and pneumoperitoneum failed to close the cavity (Fig. 22) and clinically she was getting worse. Sputum was persistently positive for tubercle bacilli. A left-sided extrapleural pneumothorax was performed on Jan. 22, 1946 (Fig. 23). The cavity was closed and has remained closed to this day—four and a half years later. The disease in the right lung has also improved (Fig. 24). She is working, and at present is contemplating marriage.

Two of the four patients presented a particularly trying problem—not only did they have large cavities which failed to close under conventional treatment, but the contralateral lungs were also badly diseased and under treatment, one with intrapleural pneumothorax, the other with extrapleural. Extrapleural was successfully established in each instance and the hilar cavities greatly reduced in size, but the extrapleural collapse had to be abandoned within the first week for lack of sufficient cardiorespiratory reserve, largely because of the extensive collapse required to close hilar cavities. The very mobilization of the cavity wall from its attachment in the vertebral gutter, however, was of considerable help and the cavity subsequently closed in one case (in the patient with a contralateral pneumothorax) and has remained smaller in the other.

COMPLICATIONS IN PATIENTS WITH SUCCESSFUL OPERATIONS

It will now be of interest to review the ninety-one consecutive successful operations (eighty-eight patients, three bilaterals) as a group.

It has already been indicated that a successful operation does not necessarily imply that all patients are alive and well. In fact, ten of the patients are dead at this writing. These deaths, however, cannot be attributed to the operative procedure. The only reason for including them at all at this time is to round out the presentation. This is made clear from the following causes of death:

Six have died from uncontrolled tuberculosis elsewhere as follows: tuberculosis of larynx, two; tuberculosis of intestines, three; tuberculous meningitis, one. These patients were operated upon in the early years of this study before streptomycin became available, and some of the deaths probably could be prevented today. Four are dead from nontuberculous causes as follows: one from hypertension and stroke, one from peritonitis following ruptured appendix, one from heart disease, and one from nephritis.

It is important, on the other hand, to emphasize again that a successful late result does not mean that no important postoperative complications were encountered. In fact, troublesome and potentially serious complications were

present in 49.4 per cent in this series, or in practically every other patient. Five important problems which had to be faced are worth commenting upon briefly at this time (Table II).

1. *Tuberculous Extrapleural Empyema.*—Tuberculous empyema of the extrapleural space, that is, cloudy or purulent fluid containing tubercle bacilli, was a rather common complication. It was present at one time or other in twenty-seven extrapleural spaces (29.6 per cent) in this series with a successful late result. In nine patients the empyema was acute and troublesome for a while. However, the acute phase passed with treatment and the empyema did not defeat the ultimate objective of the operation. In the end, the empyema cleared, apparently for good, in sixteen of the twenty-seven empyema cases, or in 59.2 per cent, and persisted in some form in eleven, or 40.8 per cent.

The occurrence of tuberculous empyema was not necessarily related to the severity or extent of the tuberculosis in the operated lung. It was entirely absent in some far-advanced cases, and, on the other hand, proved troublesome in patients with comparatively much less disease.

Tuberculous empyema of the extrapleural space is the direct result of subpleural tubercles opening their contents into the extrapleural space and contaminating it the same as in intrapleural pneumothorax and, to a large extent, is unavoidable. Streptomycin and para-aminosalicylic acid have reduced the incidence and severity of tuberculous empyema, but have not entirely prevented it. The more serious empyemas in this series have, for the most part, occurred before streptomycin became widely available.

In general, extrapleural tuberculous empyema is much less serious and more easily handled than a tuberculous empyema complicating an intrapleural pneumothorax.

The probability of tuberculous empyema complicating the operation is in itself not a contraindication to the operation. The overriding objective is to control the tuberculosis in the diseased lung and to treat the empyema as it occurs. It is the disease in the lung which kills the patient and not the tuberculous empyema. In fact, the presence of nontoxic tuberculous fluid in the extrapleural space was not incompatible with well being or good working capacity in the patients in this series. Furthermore, with new and better drugs to suppress or kill the tubercle bacillus, the potential seriousness of the empyema becomes progressively less.

2. *Intervening Reopening of Cavity.*—In five patients (5.5 per cent), the cavity reopened after it was closed and kept closed for an indefinite time. Too hasty a lengthening of the refill interval (three cases), or too early a conversion to oil (two cases) with consequent reexpansion of the lung underneath the oleothorax were the responsible factors. The good results of the operation, however, was saved by shortening the refill interval to twice a week. In the cases with oleothorax the oil was removed first.

3. *Delayed Healing of Extrapleural Wound.*—Delayed healing of the wound due to tuberculous infection occurred in eight cases, or 8.8 per cent.

TABLE II. COMPLICATIONS IN 91 CONSECUTIVE SUCCESSFUL EXTRAPLEURALS*

		NO.	PERCENTAGE
1. Tuberculous empyema		27	29.6
(With acute phase	9)		
a. Persists but not troublesome	11 (40.8%)		
b. Cleared	16 (59.2%)		
2. Intervening opening of cavity		5	5.5
3. Delayed healing of wound (Tuberculous)		8	8.8
4. Sudden loss of space		3	3.3
5. Movable upper mediastinum		2	2.2
Total		45	49.4

*Important and potentially serious complications may be expected in practically every other patient with an extrapleural operation. Postoperative management and follow-up are difficult and exacting, hardly to be compared with that of thoracoplasty.

This required persistent and patient handling. In time, however, the wounds healed and the late result of the operation was excellent.

4. *Sudden Loss of Space Postoperatively.*—For one reason or another, such as uncontrolled cough or unexpected loss of air through operative wound, the extrapleural space may occasionally be lost without warning and the lung readhere firmly to the chest wall. This occured in three cases in this series, or 3.3 per cent. Reoperation within the first two weeks and freeing of the lung proved successful. The second mobilization of the lung was well tolerated. It was not a strenuous procedure and should be resorted to if necessary without hesitation (see Case history 8).

5. *Moveable Upper Mediastinum.*—This was encountered in two patients in this series. The cavity which was left adherent to the upper mediastinum did not close for two and three months, respectively, after operation, until the upper mediastinum had become fixed. It was a trying complication and required patience.

There were other complications in this series of minor importance such as subcutaneous emphysema or excessive bleeding into the extrapleural space; however, since they presented no particular problem, they will not be elaborated upon.

FATE OF EXTRAPLEURAL SPACE IN SUCCESSFUL OPERATIONS

There has been much discussion as to the fate of the extrapleural space and whether extrapleural pneumothorax is a reversible or irreversible collapse. These and other questions that come to mind must still go unanswered. There are no reports in the literature on voluntarily reexpanded healed lungs achieved with extrapleural pneumothorax, and none are recorded in this paper. Contrary to accepted belief, however, in most cases the lung, after an extrapleural pneumothorax tends to reexpand, even when kept under collapse for long periods of time. This has been true in this series even in the face of a complicating tuberculous empyema and after a maintenance oleothorax. One of the big problems has been to hold the collapse, and frequent refills, particularly during the first year, were necessary. Extrapleural collapse, therefore, must be looked upon as potentially reversible.

TABLE III. FATE OF SPACE IN 91 SUCCESSFUL EXTRAPLEURAL OPERATIONS*

	NO.	PERCENTAGE
1. Maintained as air space (1 bilateral)	68	74.7
2. Converted to oleothorax (2 bilateral)	16	17.6
3. Collapse maintained with extrapleural fluid	7	7.7

*Contrary to accepted belief, most extrapleural lungs tend to reexpand, even when kept under collapse for long periods of time. This has also been found true in a few instances where the lung has been kept collapsed with oil and the oil subsequently removed. Extrapleural collapse, therefore, must be looked upon as potentially reversible.

As to the fate of the ninety-one extrapleural spaces in the present series of successful operations, it is as follows (Table III):

1. Sixty-eight (74.4 per cent) have been maintained as a pneumothorax (one bilateral).

2. Seven (7.7 per cent) have been maintained with extrapleural fluid coagulum. This fluid is not increasing, and seldom requires aspiration. In three, this has been true for nine, ten and eleven years, respectively.

3. Sixteen (17.6 per cent) spaces have been converted to oleothorax and require only periodic observation. Two patients have bilateral oleothorax. A highly refined grade of heavy mineral oil, introduced in small quantities at the end of each pneumothorax refill over an extended period of time, is a satisfactory means to convert an extrapleural pneumothorax into a more permanent form of selective collapse. The oil can remain in the space indefinitely (more than ten years bilaterally in one patient in this series, Fig. 15) without harmful effect. This experience is similar to that reported by Grof, Alarcon, and others.

COMMENT

Extrapleural pneumothorax fills a distinct gap in the collapse therapy of pulmonary tuberculosis not covered by other surgical procedures. It has definite indications and covers a field of usefulness all its own. It offers collapse to the more extensively advanced patient who formerly could not have been considered for any type of collapse measure. In other instances it can bring about recovery and render positive sputum negative for tubercle bacilli when other measures have failed or are too risky. Extrapleural pneumothorax, therefore, has an assured place in the therapy of pulmonary tuberculosis, independent of other measures.

However, postoperative management and follow-up are difficult, and exacting, and full of pitfalls, hardly to be compared with that of thoracoplasty. Complications are common and can be serious. For these reasons, extrapleural pneumothorax should not be undertaken lightly, but once indicated, the operation should be performed without hesitation.

PART II

ANALYSIS OF OPERATIVE FAILURES AND OPERATIVE DEATHS IN EXTRAPLEURAL PNEUMOTHORAX

Now that the positive achievements of the operation and the importance of extrapleural pneumothorax as an independent collapse measure have been

presented, it will be in order to discuss in some detail the operative failures and operative deaths encountered in this series, and the lessons they teach, and to suggest certain improvements in operative technique and follow-up, which, it is hoped, will materially increase the percentage of good results in the future.

ANALYSIS OF TWENTY-ONE UNSUCCESSFUL OPERATIONS

In twenty-one patients in this series (16.2 per cent), the operation is classified as unsuccessful for the following reasons (Table IV):

1. *Failure to close cavity:* In three patients the cavity was never fully closed following the extrapleural because of inadequate and improper stripping at the time of surgery. In one patient the operation was repeated and the cavity closed, but the wound, which was tuberculous, never fully healed, in spite of streptomycin and other measures.

2. *Reopening of closed cavity:* In nine patients the cavity was closed, and the postoperative result was excellent. As time went on, however, reexpansion of the lung, with some loss of the extrapleural space, set in and the cavity reopened and remained open. This can be attributed to (a) improper and inadequate stripping at the time of operation (four cases), (b) postoperative difficulty in maintaining adequate collapse because of coagulated extrapleural fluid (three cases), or (c) too soon a lengthening of refill interval (two cases).

TABLE IV. TWENTY-ONE UNSUCCESSFUL EXTRAPLEURAL OPERATIONS (16.2 PER CENT) IN 129 CONSECUTIVE OPERATIONS*

CAUSE		NO.	PERCENTAGE
1. Failure to close cavity		3	14.3
a. Improper stripping			
2. Reopening of closed cavity		9	42.9
a. Improper stripping	4		
b. Fluid coagulum	3		
c. Too long refill interval	2		
3. Abandoned		4	19.0
a. Poor vital capacity	2		
b. Cough (tuberculous larynx)	2		
3. Empyema (mixed infection)		3	14.3
4. Poorly healed wound (tuberculous) (Tuberculous thoracic fistula)		2	9.5

*The percentage of unsuccessful operations in future series can be reduced to less than 5 per cent through improved operative technique, use of antibiotics and chemotherapeutic agents, and exacting and continued control of the extrapleural space.

3. *Abandonment of extrapleural space:* In four patients, the extrapleural operation was satisfactory technically, but the collapse was subsequently abandoned. In two, it was done voluntarily within one week after operation because of inability of the patient to accommodate to the required collapse. Both patients were poor risk cases. They had bilateral disease and contralateral collapse, with the cavities in the extrapleural lung located in the apex of the lower lobe. Such cavities, because of their location, require extensive collapse of the lung—more than these patients could tolerate. Their case histories were briefly discussed above under hilar cavities. In the other two, the extrapleural collapse had to be abandoned as a bad job because of persistent and

uncontrolled cough, the result of a troublesome tuberculous laryngitis. The lung just couldn't be kept down, and after a while it readhered to the chest wall. This occurred before streptomycin became available.

4. *Mixed infection empyema of extrapleural space:* This accounted for three failures. They all occurred before penicillin and streptomycin became available. The space was successfully obliterated in two with thoracoplasty. The third patient is reasonably well, but extensive disease in the contralateral lung makes thoracoplasty impractical.

5. *Poorly healed wound (tuberculous thoracic fistula):* Poor healing of the wound because of tuberculous infection after a successful operation with closure of cavities occurred in eight patients in this series. In six, the wound healed in time and did not interfere with a successful outcome. In two, however, the wound has remained troublesome, with reopening of the cavity in one because of inability to maintain the collapse.

COMMENT

When one analyzes the above complications and reevaluates them in the light of improved technique (to be discussed below) and the availability of modern drugs, it becomes at once apparent that fifteen of the failures in this series were essentially preventable, for they had their origin either in faulty technique (twelve cases) or unavailability of antibiotics at the time of surgery (three cases). This means that at least 71.5 per cent of the complications in this series were theoretically preventable, and that the over-all risk of an unsuccessful result can be reduced in future series to less than 5 per cent.

ANALYSIS OF THE SEVENTEEN OPERATIVE DEATHS

As stated, there were seventeen operative deaths in this series from all causes, both early and late, an over-all operative mortality of 13.2 per cent made up as follows (Table V):

1. *Poor cardiorespiratory function:* Eleven of the deaths, or 64.7 per cent, were cardiac in origin in the sense that the heart simply could not accommodate itself to the extra demand thrown upon it by the extrapleural collapse, and gave way, resulting in death. All deaths occurred within the first two weeks of surgery. The primary fault was poor cardiorespiratory reserve, underestimated at the time of surgery. The cases fall into the following subgroups:

(a) *Patients with clinical dyspnea and poor physical condition.* In eight, not only was the disease extensive and bilateral, but their physical condition was poor, and dyspnea was noticeable clinically before operation on ordinary exertion. These were desperate cases, all "used up" clinically. Surgery was undertaken as the final, forlorn hope for the patient. While much has been learned in the handling of this type of case, in retrospect, at least five of these patients would not be accepted for surgery today, as beyond hope. They were included early in this series when limitations of the operation had to be learned first-hand.

TABLE V. SEVENTEEN OPERATIVE DEATHS (13.2 PER CENT) IN 129 CONSECUTIVE OPERATIONS*

CAUSE		NO.	PERCENTAGE
1. Poor cardiorespiratory function		11	64.7
a. Poor selection of case	8		
b. Over collapse	2		
c. Unrecognized hemorrhage with pressure on mediastinum	1		
2. Vagal reflex irritation (?)		1	5.9
3. Mixed infection empyema		3	17.6
a. Acute	1		
b. Chronic	2		
4. Broncho-pleural fistula		2	11.8
a. Tear	1		
b. Erosion (Progressive disease)	1		

*More than two-thirds of the above deaths are preventable through better selection of cases, use of antibiotics and improved operative technique. Operative mortality under such conditions should not exceed an estimated 4 per cent. In fact, in the last sixty-five consecutive operations, with liberal indications for surgery, it was 1.6 per cent.

(b) Two deaths were in patients with fair to poor cardiorespiratory reserve, but in better clinical condition than those included under (a). Perhaps, in retrospect, these deaths might have been prevented, had the collapse been pushed less energetically and more time given for the heart to accommodate.

(c) One patient, with fair to poor cardiorespiratory function, died rather suddenly on the ninth postoperative day. He was doing well until then. At post mortem the extrapleural space was found filled with fresh blood and fibrin clots from recent hemorrhage. The hemorrhage was unrecognized clinically. However, it was appreciated at the time that there was increased pressure on the mediastinum, but attempts at aspiration were unsuccessful because of fluid coagulum. Had aspiration been successful and the pressure on the mediastinum relieved, in all probability, death could have been prevented, as the actual blood loss was not severe.

2. *Vagal reflex irritation:* One death, apparently cardiac in origin, occurred in 1943, eighteen hours after surgery. Death came suddenly and without apparent explanation. There was no bleeding and no over-collapse (Fig. 26). Unfortunately, there was no post mortem. However, in this patient the mesial aspect of the lung was stripped down to the hilum, as was the custom at the time. It was felt that this had something to do with the sudden fatal outcome. Transient electrocardiographic changes resembling coronary occlusion had been observed in other patients early in this series following stripping from the mesiastinum, presumably from vagal irritation. In fact, in one patient there was actual cardiac arrest but with recovery from vagus reflex at the time of stripping from the mediastinum. Since 1943, the mesial aspect of the lung has been left attached to the upper mediastinum, and these troublesome complications have not again been encountered.

3. *Empyema of extrapleural space:* Three deaths were the direct result of mixed infection empyema of the extrapleural space. One empyema was acute, with death within three weeks, and two were chronic, with death fourteen and twenty-nine months after surgery from progressive tuberculosis and general deterioration in health. These operations were carried out in 1939 and 1940,

respectively, before penicillin and streptomycin were available. There have been no operative deaths directly or indirectly attributable to infection of the extrapleural space since modern antibiotics have become available. Empyema of the extrapleural space, tuberculous or otherwise, can either be prevented or handled satisfactorily if it does occur.

4. *Broncho-extrapleural fistula:* One death occurred early in this series (1939) from a traumatic broncho-extrapleural fistula, the direct result of tearing the lung in stripping from the chest wall. Death occurred within three weeks after surgery. Improved operative technique in stripping firmly adherent lung is the answer to this complication. If stripping is considered too hazardous, the operation should be abandoned.

Traumatic broncho-pleural fistula must be differentiated from that due to erosion, the direct result of progressive disease. Erosion fistula occurred in only one case in this series, in 1941, in a patient with caseopneumonic tuberculosis. The operation was technically successful, and the patient showed gratifying continued improvement for the next three months. Antibiotics, however, were badly needed to control the acute character of the disease until such time as the collapse could take full hold. As it was, the disease in time eroded the lung, and the patient subsequently died under thoracoplasty. This complication has not recurred since streptomycin has become available.

There were no deaths from sloughing or "blow-out" of the cavity wall in this series, although patients with cavities larger than 4 cm. in diameter and peripherally located were included.

COMMENT

Sixteen of the above seventeen deaths occurred between 1938 and 1946, inclusive, in the course of sixty-four consecutive operations (94.1 per cent), and one death between 1947 and May, 1950, inclusive, in the course of sixty-five consecutive operations (1.5 per cent). More than two-thirds of the deaths (68.7 per cent) were cardiac in origin, the result of poor cardiorespiratory reserve underestimated at the time of surgery. The more impressive record since 1946 is attributed largely to a better selection of patients, to improved operative technique, and to the liberal use of antibiotics and chemotherapeutic agents.

A low operative mortality, however, while highly desirable, is not enough. If extrapleural pneumothorax is to serve its full purpose, one must be liberal with indications for surgery, for the alternative is to let these tuberculous patients die of progressive disease. A large factor of personal equation and enthusiasm must, therefore, enter into the selection of advanced cases for extrapleural surgery, and this, in turn, will reflect itself in operative mortality. Even so, operative mortality can be reduced to less than 4 per cent.

PART III

SUGGESTED IMPROVEMENTS IN OPERATIVE TECHNIQUE AND FOLLOW-UP

Experience has shown that many of the deaths and complications encountered in the 129 consecutive operations, particularly in the first years of this

study, can be prevented today, or handled satisfactorily if they do occur, and the percentage of good results, therefore, materially improved in future series. It is in this spirit that the following suggestions are made:

1. *Proper selection of patients:* Although liberal indications should prevail when selecting patients for the extrapleural operation, one should stop short of the obviously doomed patient with poor cardiorespiratory function. This common sense contraindication will go a long way in reducing operative mortality. The operative procedure itself is not shocking and, theoretically, should carry a low operative mortality. The unknown factor, of course, is the *quality* of the cardiorespiratory reserve in the far-advanced case with bilateral disease and in poor physical condition. Present-day functional studies are not sufficiently reliable. It was amazing to see poor risk patients, with preoperative vital capacity studies of 50 per cent or less, tolerate this procedure quite well and obtain good results. The best guide, in my experience, has been the clinical impression of the patient. If the patient was dyspneic clinically, on ordinary exertion, the result of long-standing and extensive disease, he was a very poor risk. Two-thirds of the deaths in this series were in this type of patient. Such cases are better excluded from surgery, as beyond help. Less desperate cases, however, should not be denied the potential benefits of extrapleural surgery if the overall prospects for recovery with collapse are reasonably good. In other words, indications should be liberal, but reasonably so, with the thought in mind that the extrapleural operation is intended for the substandard risk case with an otherwise poor prognosis. Under such conditions, operative mortality should not exceed 4 per cent.

2. *Planned use of antibiotics and chemotherapeutic agents:* Intelligent use of modern antibiotics and other chemotherapeutic drugs, such as para-aminosalicylic acid, both pre- and postoperatively as part of a planned treatment, has made a vital difference in extrapleural surgery. These drugs have literally saved this operation. It has been my practice to introduce 200,000 units of penicillin, 1 Gm. of streptomycin, and 10 c.c. of 20 per cent solution of para-aminosalicylic acid into the extrapleural space daily during the first postoperative week, then every other day during the second week and twice weekly thereafter until fluid no longer accumulates. This is in addition to whatever drug therapy the patient is to receive by other channels. There has been a decided reduction in the number and severity of tuberculous empyemas encountered under this regime. Secondary infection of the extrapleural space has been entirely eliminated.

3. *Careful mobilization of lung:* As stated above, broncho-extrapleural fistula may result from trauma in stripping the lung from the chest wall. This can be prevented by careful operative technique. The finger is not always a safe guide in determining resistance to stripping, and may penetrate the lung. Where difficulty is encountered, a better method is to use a gauze sponge on the end of a long curved forceps. The protected end of the forceps is carefully maneuvered, under direct vision, between lung and chest wall with the pressure of the sponge exerted in the direction of the chest wall. The lung is thus carefully brushed off. If too much resistance is encountered at one point, the

attempt is temporarily given up and another area attacked. The point of resistance is thus isolated and often handled satisfactorily by further manipulation of the sponge forceps. In more difficult cases, the periosteum on the under surface of the rib is loosened and carried away with the adherent part of the lung, a sort of localized internal periosteal stripping. Alarcon has described a somewhat similar method in his recent book. Extensive stripping of firmly adherent lung can thus be accomplished with relative safety.

4. *Proper and adequate stripping:* Some cavities in this series were never closed, others closed only to reopen weeks or months later. In retrospect, this was found to be due to improper and inadequate stripping at the time of initial surgery.

The stated objective of extrapleural pneumothorax for the surgical collapse of upper lobe tuberculosis is to create an ideal selective pneumothorax, one which will result in complete collapse of the diseased area of the lung with little disturbance to the healthy portion. To accomplish this, it is common practice to mobilize completely the upper lobe at the time of operation. The upper half of the lung is stripped not only from the chest wall, but also mesially from the upper mediastinum. This results in both lateral and vertical collapse, and by this procedure the apex is usually dropped to the level of the hilum. It is believed that this type of mobilization closely approaches the ideal intrapleural pneumothorax.

Clinical experience, however, has not borne this out, for unclosed cavities followed this type of mobilization in a significant percentage of cases, 5.4 per cent in this series.

Characteristics of the extrapleural space: Conditions in a free intrapleural pneumothorax space and in an artificially created extrapleural space are not the same. In an intrapleural pneumothorax, the entire lung is usually free. There is give and take to the collapse. It can be increased or decreased at will. Furthermore, the interplay of forces, namely, the difference between intrapulmonary and intrapleural pressures and the altered elasticity of the diseased lung, which together are largely responsible for the creation of the selective pneumothorax, have free sway, and the lung reshapes itself accordingly. Unless pleural adhesions or improper technique prevent, the healthy portion of the lung invariably remains expanded and in use; the diseased part well collapsed and virtually functionless.

But such conditions are not present in the artificially created extrapleural space. The uncollapsed portion of the lung remains firmly adherent to the chest wall; there is no give and no reshaping of the lung, as in intrapleural pneumothorax. Once the upper lobe is mobilized and freed from its mediastinal attachment, it can go in only one direction, downward and toward the hilum (Figs. 25, 26). The conditions thus created are analogous to the Semb apicolysis in thoracoplasty. In the latter, it was soon found that in many instances the apical cavity was not closed, but merely displaced downward to the hilum level and that more extensive surgery was ultimately needed to close such displaced cavities. This is aside from the increased operative risk

of stripping the lung from the mediastinum with possible injury to large vessels and nerves and the danger from ventricular fibrillation from too violent traction on pleuro-pericardial adhesions.

The same holds true in extrapleural pneumothorax if the upper lobe is stripped from the mediastinum. While small cavities may close, cavities three centimeters or more in diameter are often displaced downward and toward the hilum rather than closed. Increased extrapleural pressure above the area of collapse only depresses the cavity still lower, but does not necessary close it (Fig. 26).

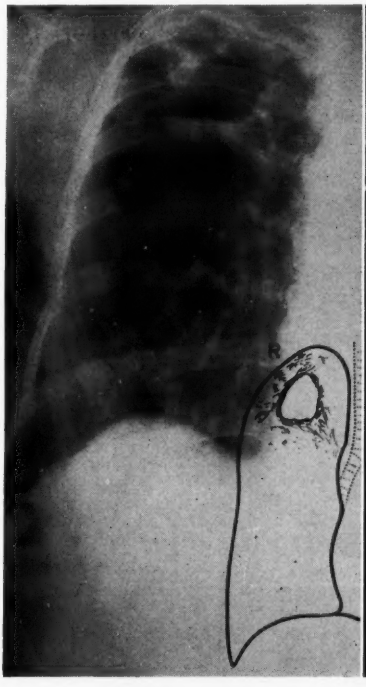

Fig. 25.

Fig. 26.

Fig. 25.—M. M. Large cavity in right upper lobe.

Fig. 26.—M. M. Twenty hours after extrapleural pneumothorax operation. The upper half of the lung has been stripped completely, extrapleurally, from chest wall and upper mediastinum. Note the new position of the cavity, now located at the hilum level, and that the cavity still remains open, even though two air refills have been administered since operation.

Even if the cavity should close soon after the mediastinal mobilization, it may reopen later. As the stripped lung gradually reexpands, it readheres to the upper mediastinum and chest wall in an uneven circular manner, and the cavity can be pulled open. In such cases, the reopened cavity remains suspended midway between mediastinum and chest wall (Figs. 27, 28, 29) and may necessitate extensive thoracoplasty for its closure.

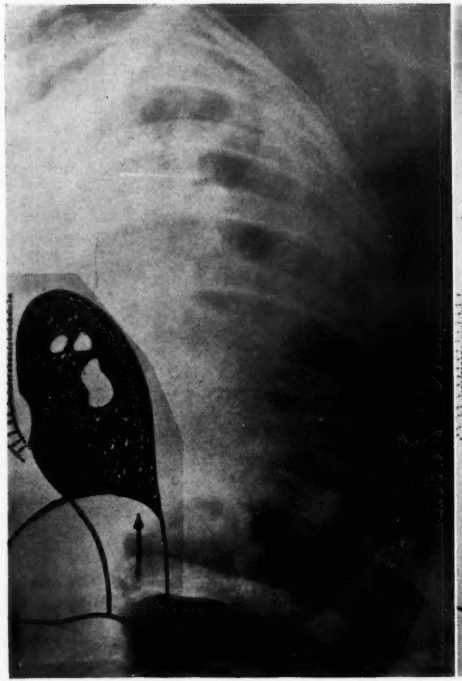

Fig. 27.

Fig. 28.

Fig. 29.

Fig. 27.—B. E. Feb. 2, 1942. Extensive exudative disease throughout left lung with multiple cavities in upper lobe. The disease failed to respond to bed rest, phrenic nerve interruption and pneumoperitoneum therapy. Pneumothorax was ineffective and streptomycin was not available at the time.

Fig. 28.—B. E. May 29, 1942. Planigram study after successful extrapleural operation indicates excellent collapse of upper three-fourths of left lung with all cavities closed. The upper half of the lung in this case was stripped extrapleurally from chest wall and mediastinum with the apex of the upper lobe dropped to the level of the hilum. Sputum negative.

Fig. 29.—B. E. Aug. 17, 1942. Approximately three months later. The left lung has partially reexpanded from below upwards, reattached itself to the chest wall, in spite of frequent air refills and one of the cavities has reopened. The apex of the upper lobe still remains at hilar level. This complication is much less likely to occur when the upper lobe is *not* stripped mesially, but is allowed to remain adherent to the upper mediastinum.

Importance of not mobilizing mesial aspect of lung: To obviate this failure of open cavity following extrapleural pneumothorax, it is essential to alter the technique of extrapleural mobilization in two directions. In the first place, the mesial surface of the lung should *not* be stripped from the mediastinum. The apex can and should be moved down to or below the level of the clavicle to obtain some vertical collapse to reduce the possibility of a slit cavity, but the remainder of the mesial surface of the lung must be allowed to remain attached to the upper mediastinum. This gives a firm surface against which

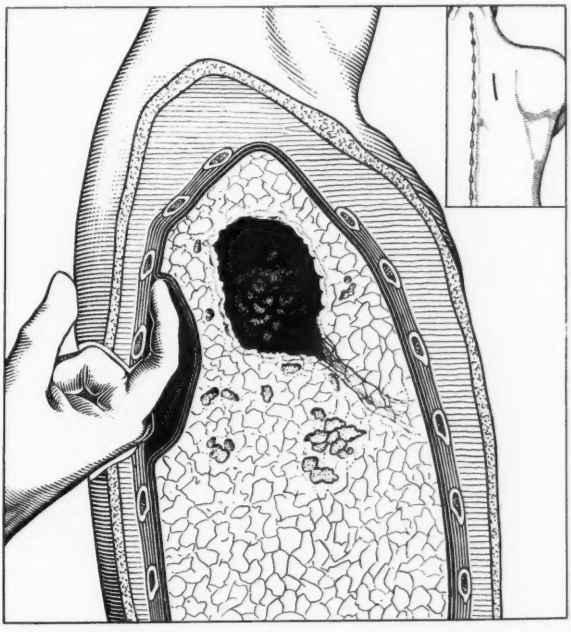

Fig. 30.—Initial Stripping of Lung: Mobilization is begun posteriorly after resection of approximately four centimeters of the fourth or fifth posterior ribs through a small (5 to 8 cm.) paravetebral incision (see insert). The small incision is important as it minimizes the chances of wound disruption from a possible complicating tuberculous empyema or from positive pressure refills. Mobilization is begun in the vertebral gutter and is carried forward towards the mediastinum. Pressure of the finger tip is directed towards the chest wall and away from the lung. A long curved forceps tipped with a small sponge is used beyond the reach of the finger.

to collapse the cavity, the mediastinum acting as a sort of anvil, and the pneumothorax refills as the hammer. In the presence of a mobile upper mediastinum, the mediastinum in time will become fixed and the cavity will close. The collapse thus created is largely lateral, toward the mediastinum. All cavities which can close will close by this procedure.

Furthermore, by eliminating stripping of the lung from the mediastinum, one of the real potential hazards of extrapleural pneumothorax is also eliminated.

The second innovation in technique follows logically from the first. If the medial surface of the lung is not to be disturbed, then stripping of the lung from the remainder of the chest wall must be *more* extensive than is usually practiced to permit collapse of the cavity-bearing lung laterally toward the mediastinum (Figs. 30, 31, 32).

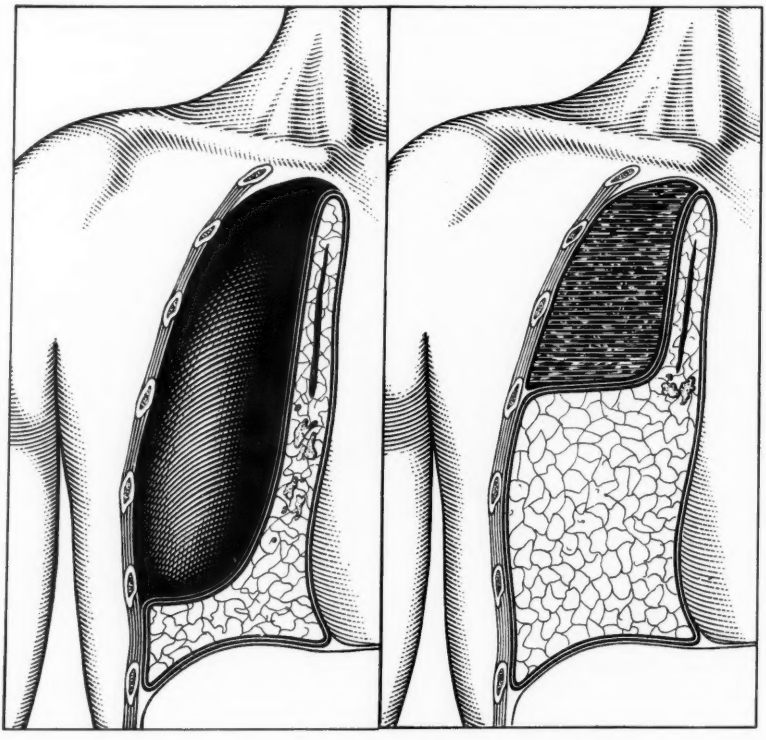

Fig. 31. Fig. 32.

Fig. 31.—Extent of Mobilization: For reasons mentioned in the text, mobilization at the time of operation must be extensive, but should not include the mesial surface of the lung. The apex, however, is dropped to below the clavicle. Stripping should be carried downward one or two ribs below the level of demonstrable disease. In patients with advanced disease, this usually means as far down as the eighth or ninth posterior rib and the fourth rib anteriorly.

Fig. 32.—Selective Extrapleural Oleothorax: After one is certain that all cavities are closed, the disease in the collapsed lung controlled and no undesirable complications such as tuberculous empyema present, the collapse can be made highly selective and localized to any desired degree. The pneumothorax pocket can then be replaced, if desired, by a more solid medium. In practice, mineral oil is the best of all foreign substances with which to maintain the collapse created by the extrapleural pneumothorax operation.

The potential collapse created at the time of operation should be at least one or two ribs below the area of demonstrable disease, which usually means in far-advanced cases as far down as the eighth or ninth ribs posteriorly and to the fourth costosternal junction anteriorly (Fig. 31). In patients with strictly limited disease and with small cavities, stripping from the chest wall can stop at the level of the sixth or seventh posterior rib and the third rib anteriorly.

Extensive stripping from the chest wall, as described above, is important not only for the technical reason already stated, namely, to make it possible for the upper half of the lung to be collapsed laterally toward the mediastinum, but also to allow for some loss of extrapleural space, which invariably happens in almost all cases before the cavity is actually closed. By creating more immediate collapse than is ultimately needed, one automatically compensates for this contingency and thus assures the operator sufficient maneuverability and time postoperatively to close all cavities. After it is established with certainty that the cavities are closed and the disease controlled, reexpansion of the lung may be permitted from below upward, and the collapse localized and made highly selective (Fig. 32).

The extensive mobilization at the time of operation advocated above need not prove embarrassing to the patient. It is not necessary to collapse immediately and completely the mobilized lung in order to prevent readherance to the chest wall. Complete collapse of the mobilized portion can be brought about gradually over a period of weeks if necessary, and thus give ample time for accommodation to the collapse.

5. *Use of streptokinase and streptodornase:* Serosanguineous postoperative fluid in the extrapleural space was present in virtually every case in this series. It usually developed on the second postoperative day. Simple aspiration and irrigation of the space with saline repeated a few times was all that was found necessary to correct this in the majority of cases. In some, however, the fluid became quite a problem; in three cases it defeated the ultimate purpose of the operation, for it resulted in open cavity.

What happened was that fibrin bodies and fluid coagulum formed in the extrapleural space and interfered with aspiration. Furthermore, as more fluid formed, alarming symptoms of mediastinal pressure would supervene, necessitating strenuous efforts at relief. Once this difficulty was overcome, the fluid coagulum acted as a barrier to the pneumothorax, favored obliteration of the space, and reexpansion of the lung, with consequent reopening of the cavity, even months after a successful operation.

Until now little could be done about these problems except for repeated washing and aspiration of the extrapleural space and reducing the interval between refills or remove the material surgically as advocated by Alarcon. Recently, however, I have used streptokinase and streptodornase to solve these problems, with graitfying results.[13] These enzymes dissolve the fibrin bodies and fluid coagulum, and accomplish an enzymatic debridement.

Within twelve hours after its introduction into the extrapleural space, the fluid becomes free-flowing and is easily removed (Figs. 33, 34, 35). Caution, however, in its use is essential, for it may precipitate serious oozing if used too soon postoperatively. Also it has been found to speed up the pulse rate and thus embarrass the heart at a time when it is already under strain.

In the presence of an obliterating extrapleural space, streptokinase and streptodornase apparently may dissolve the fluid coagulum between lung and

chest wall responsible for the obliteration, and thus makes possible an increase in collapse (Figs. 36, 37). Streptokinase and streptodornase also help to liquify thick tuberculous fluid if present. A more detailed report will follow.

6. *Proper spacing of refills:* Improper spacing of refills may lead to premature reexpansion of the lung and consequent reopening of the cavity. It is better to give small quantities of air—100 c.c. or less—often, once or twice a week at first, and to maintain a short refill interval for at least the first year.

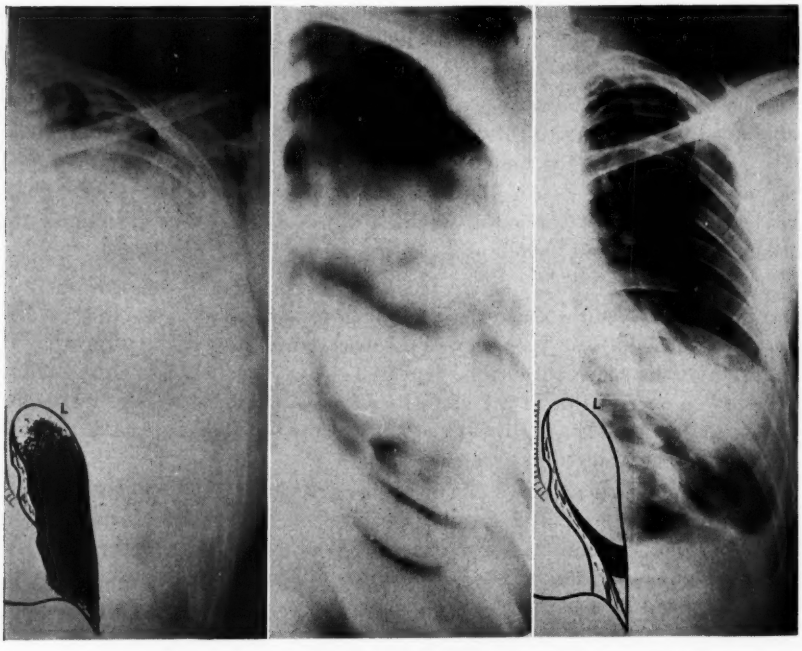

Fig. 33. Fig. 34. Fig. 35.

Fig. 33.—G. K. Forty-eight hours after extrapleural. Entire left chest filled with fluid coagulum. Aspiration difficult.

Fig. 34.—G. K. Planigram after many attempts at aspiration. Note pockets of fluid coagulum.

Fig. 35.—G. K. The fluid coagulum has been liquefied and aspirated after use of streptokinase and streptodornase, revealing extent of extrapleural pneumothorax.

This is the vital year. Most of the resolution of reversible disease takes place during this time, and every effort should be made to hold most of the collapse created at the time of surgery. Contrary to accepted belief, there is little danger of the collapsed extrapleural lung not reexpanding. It usually works the other way.

7. *Small and strong operative wound:* A relatively small and strong operative wound is important to avoid future trouble inasmuch as one is always working with positive extrapleural pressures, at times in the presence of tuber-

culous fluid. The smaller the wound and the more air-tight the closure, therefore, the less likely the chance for tuberculous infection and mechanical rupture of the wound.

The best approach is posteriorly midway between the vertebral border of the scapula and the spine (Fig. 30). Most of the difficulty in stripping is posteriorly where the disease is. The incision need not be longer than 6 or 8 centimeters.

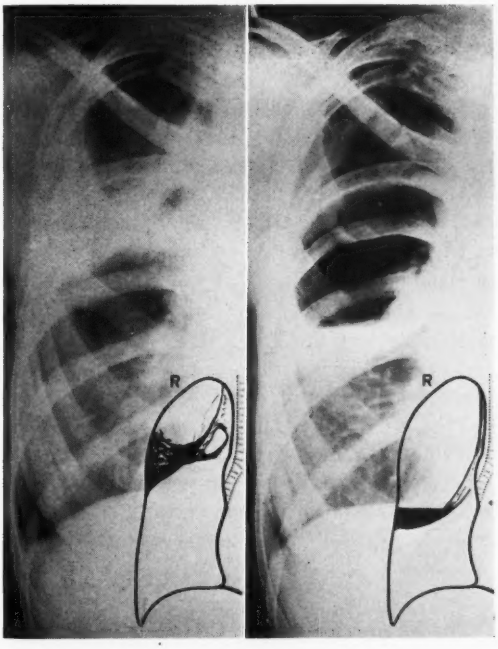

Fig. 36. Fig. 37.

Fig. 36.—J. P. Gradually reexpanding left lung with reopening of cavity underneath bridge of fluid coagulum following successful extrapleural pneumothorax twenty-one months previously, in spite of frequent air refills.

Fig. 37.—J. P. Two weeks later. Reestablishment of extrapleural collapse and closure of cavity following use of streptokinase and streptodornase.

Proper closure of the wound is essential to a good result, and the first layer of muscle closure is the most important. The spinal muscles and lumbodorsal fascia which have been split at the angle of the ribs and retracted in exposing the ribs are sutured to overlap the approximated intercostals. This makes for good firm support, and the wound usually becomes air-tight with this first layer. The other muscle layers add additional strength and support. There have been no difficulties with wound healing since adopting the above procedure.

8. *No immediate plombage:* Any discussion of extrapleural pneumothorax technique inevitably brings up the controversial question of immediate plom-

bage. This question is timely because of the interest aroused by the recent use of lucite balls, fiber glass wool, and plastic sponges with which to maintain the collapse.

From the very first it was felt desirable to pack the extrapleural space with a suitable foreign body at the time of operation and thus avoid subsequent frequent air refills. Invariably such efforts have failed. In 1935 I reported experiments with an agar-agar compound which proved successful in a few cases.[14] As I gained experience with this phase of the procedure, however, I became convinced that the principle of introducing a foreign body at the time of operation to maintain the collapse is wrong on several counts and should be abandoned.

In the *first* place, cavities of sufficient size to warrant thoracoplasty are seldom closed by the extrapleural at the time of mobilization of the lung. Closure is usually a matter of days or weeks and even months following operation. Certainty of cavity closure, therefore, cannot be determined at the time of operation (Figs. 26, 38). To introduce any plomb at this time is by its very nature a blind procedure which in the end may defeat the purpose of the operation.

In the *second* place, fluid invariably forms in the extrapleural space within twenty-four to forty-eight hours following operation as a direct result of the trauma from the stripping of the lung. Introducing a foreign body at this time can only add to the fluid formation. The increased fluid formation, on the other hand, is a danger in itself; for, unless the fluid is aspirated, it may result in self-stripping of the lung with attendant bleeding and more fluid formation. And so a vicious cycle can be set up. Since all of this takes place in a restricted space made more confining by the presence of foreign body (plomb), it may lead to serious pressure consequences, even death, unless corrected.

In the *third* place, tuberculous empyema develops in approximately 30 per cent of cases, and this complication needs proper treatment in itself. In the presence of plomb, adequate treatment of the empyema is impossible without first removing the foreign body.

Fourthly, since the collapse created at the time of operation is invariably more extensive than is ultimately found necessary, immediate plombage can mean only the introduction of much more foreign body than is really necessary to maintain a good selective collapse. This in itself is undesirable and brings up another very important point commonly overlooked in planning treatment for pulmonary tuberculosis, namely, the reversible character inherent in the tuberculous pathologic process.

Much of the exudative and infiltrative disease seen in a tuberculous lung can and does undergo resolution under collapse. Cavities have disappeared and left no trace. It is virtually impossible, however, to tell beforehand how much of the disease will disappear and how much will remain. Experience has shown that most of the resolution of the tuberculous process will take place within the first six to twelve months of treatment by collapse. If it is thought desirable to convert the extrapleural pneumothorax into a more permanent form of collapse without resorting to thoracoplasty, substitution with oleo-

thorax or the introduction of lucite balls or some other foreign substance is best accomplished six or twelve months *after* operation, except in the presence of a rapidly obliterating space. At the end of six to twelve months the full value of the operation has been established, the pneumothorax space reduced to the extent desired, and the collapse limited to the diseased area as it appears then. Furthermore, such troublesome complications as tuberculous empyema or bronchopleural fistula, if present, have been corrected or the operation abandoned. Plombage resorted to under these conditions becomes an independent procedure, a replacement therapy pure and simple (mineral oil is satisfactory) to maintain a highly selective collapse already established.

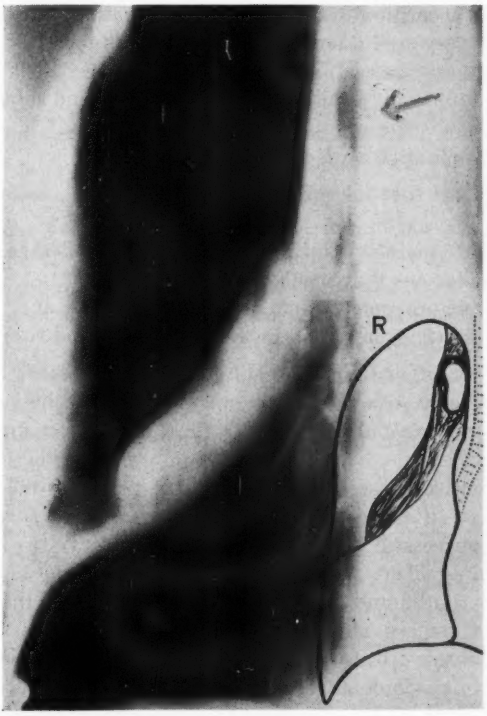

Fig. 38.—F. G. Open cavity at right apex three months after extrapleural operation. Subsequently this cavity closed and the patient made an excellent recovery (see Case 6). To have introduced lucite balls or any plomb at the time of operation would have been disasterous.

The advantages of ultimately limiting the collapse to the smallest possible area of lung compatible with a good and lasting clinical result become obvious when dealing with tuberculous patients with both lungs badly damaged and a low cardiorespiratory reserve. If there is any doubt as to the desirability of reexpanding the extrapleural lung in the future, the collapse should be maintained with air alone.

SUMMARY AND CONCLUSIONS

The immediate and late results following extrapleural pneumothorax in a single series of 121 consecutive adult tuberculous patients of approximately the same social and economic status, involving 129 operations (eight bilateral extrapleurals) performed by the author beginning in 1938, are reviewed critically. The average period of postoperative observations was fifty-four months. More than 50 per cent of the patients were under observation from three to eleven years.

Criteria are given for evaluating the results, which are believed to make possible an improved, practical approach to the subject and to help resolve the present confusion and contradictory conclusions. Cases are classified into three main groups according to the predominant character of the lesion present at the time of surgery: (1) acute caseopneumonic tuberculosis; (2) subacute exudative tuberculosis; and (3) chronic fibroulcerative. Each group is further subdivided into unilateral, predominantly unilateral, and bilateral, depending on the extent of the disease.

The paper is presented under three headings:

1. The value of the operation as an independent collapse measure in selected cases.

2. Analyses of operative failures and operative deaths encountered in this series and the lessons they teach.

3. Suggested improvements in operative technique and follow-up which it is hoped will materially improve the percentage of good results in the future.

In the interest of simplicity, results of the operations are classified as operative success, operative failure, or operative death, based on the late result obtained in the treated lung at the time this report has been prepared (June, 1950).

Taking the entire consecutive series of 121 patients, 129 operations, as a whole, irrespective of the type of patient subjected to surgery, ninety-one operations were successful (70.6 per cent), and twenty-two were unsuccessful (16.2 per cent). There were seventeen operative deaths, or 13.2 per cent. Most of the poor results and deaths, however, occurred in the earlier years of this study before modern antibiotics became available and certain technical improvements evolved. It also included patients in such obviously poor physical condition as to preclude any reasonable prospects of success regardless of treatment. Excluding such patients from future surgery, but at the same time employing liberal indications for the operation, over-all mortality can be reduced to less than 4 per cent, and operative failures to less than 5 per cent.

The experience gained from this series, considered in the light of a critical review of the literature, leads to the following conclusions:

Extrapleural pneumothorax fills a distinct gap in the collapse therapy of pulmonary tuberculosis not covered by other surgical procedures. It has definite indications and covers a field of usefulness all its own. It offers collapse to the more extensively advanced patient who formerly could not have been considered for any type of collapse measure. In other instances it can

bring about recovery and render positive sputum negative for tubercle bacilli when other measures have failed or are too risky. Extrapleural pneumothorax, therefore, has an assured place in the therapy of pulmonary tuberculosis independent of other measures.

Broadly speaking, there are several groups of patients who can be benefited by extrapleural pneumothorax:

1. Patients with advanced bilateral fibroulcerative tuberculosis who fail to respond to bedrest or sanatorium care, in whom such collapse procedures as pneumothorax, pneumoperitoneum, or phrenic nerve interruption cannot be instituted or have failed; in whom thoracoplasty is entirely too hazardous an undertaking, but who are still in fair general health.

2. Patients with acute tuberculosis not responding to conventional forms of treatment, and in whom other major surgical procedures are contraindicated or too hazardous.

3. Elderly individuals, that is, patients in the fifth and sixth decades of life with positive sputum. Extrapleural pneumothorax is often the only surgical collapse measure available for rendering the sputum negative.

4. Tuberculous patients with active disease and positive sputum, who, in addition, have special collapse problems such as hilar cavities (at times the most difficult of all to close), uncontrolled pulmonary hemorrhage, or pregnancy, which cannot be resolved by ordinary means, constitute an important and serious group. Extrapleural can bring about brilliant recoveries in some of these patients otherwise doomed.

5. Young people, particularly young women, who dread the thought of a thoracoplasty with its aftermath of psychic trauma, can frequently overcome this dilemma with extrapleural pneumothorax.

Unfortunately, following a brief spurt of popularity a few years ago in this country, this operation has lost favor in many quarters largely because of the numerous postoperative complications and poor late results encountered by early operators. But these can be overcome. The operation, of course, should not be undertaken lightly as the postoperative management and follow-up are difficult and exacting, but once indicated, the operation should be performed without hesitation.

Close attention to detail before, during, and long after the operation and planned use of modern drug therapy are the determining factors in ultimate success. In contrast to thoracoplasty, the extrapleural patient needs constant attention. Extrapleural pneumothorax is a one-man task.

Five important innovations in extrapleural pneumothorax technique are advocated.

1. The mesial aspect of the lung should not be stripped from the mediastinum.

2. Stripping from the remainder of the chest wall should be extensive, more extensive than is commonly practiced.

3. A small paravertebral incision followed by air-tight closure of the wound with the first layer of wall consisting of spinal muscles and lumbodorsal fascia overlapping the sutured intercostals.

4. No immediate plombage. The disadvantages and failures are many. Filling of the extrapleural space (mineral oil is satisfactory) when considered desirable should be an independent procedure.

5. Use of streptokinase and streptodornase in the management of postoperative extrapleural fluid coagulum and in the control of obliteration of the space.

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PATHOLOGY OF PLEURAL SCLEROSIS; A STUDY RELATED TO THE LOSS OF EXPANSIVITY OF THE LUNGS AND ITS TREATMENT

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THORACOSCOPY and the Jacobaeus operation made it necessary to obtain a better knowledge of the fibrosing reactions of the pleura. Later attempts by various investigators to produce adhesions brought a clearer understanding of the pathogenesis of this type of adhesions. The rediscovery in recent years of the surgical treatment of the nonexpansile lung has centered new interest in the study of pleural reactions.

Having at our disposal a large amount of thoracic, surgical, and post-mortem material from patients with pulmonary disease, we became interested in the study of pleural induration, and especially of the so-called pleural shell, or peel.

MATERIAL AND METHOD OF STUDY

The study was performed on the visceral and parietal pleura found in over 200 post-mortem examinations of patients with chronic pulmonary tuberculosis, and in 138 surgical specimens removed in the treatment of a great variety of conditions. In addition, the visceral pleura of over 100 dog lungs was studied after ligation had been done of a pulmonary artery, vein, or bronchus, to determine the reaction of the pleura to the mild trauma produced by the surgeons' hands. In these dogs we could observe the alterations occurring in the visceral pleura at different stages, varying from a few hours to a number of months after the operation.

All material was embedded in paraffin, and sections were stained with Mayer's Alum Hematoxylin and eosin. Other staining methods were used when required.

ANATOMY OF THE PLEURA

In order to avoid repetition of the work of Policard and Galy,[2] Letulle,[3] Vosskühler,[4] Strauss,[5] Argaud,[6] etc., to which the reader in search of a complete anatomic study is referred, the detailed anatomy of the pleura will not be considered here. However, certain details will be considered here as they are important in the better understanding of the pathology encountered.

In Fig. 1 the structure of both pleural layers may be seen, showing the difference between them. Their superficial parts are similar, being formed by the mesothelium, a thin layer of submesothelial connective tissue, and the

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internal elastic laminae. The deeper regions are notably different. Whereas the visceral pleura has a connective vascular layer which penetrates into the lung tissue via the interlobular bands, the subpleural layer of the parietal leaf forms a continuous connective layer with fatty tissue separated from the deeper layers by an elastic lamina. This layer is known as the endothoracic fascia and forms an anatomic cleavage plane which does not exist in the visceral pleura.

There is also an important point concerning the pleural epithelium. It has received a variety of names—epithelium, celothelium, mesothelium, endothelium, pleuroblast, etc.—and plays an important part in pleural pathology, and in maintaining the smoothness of the pleural surface. Together with the

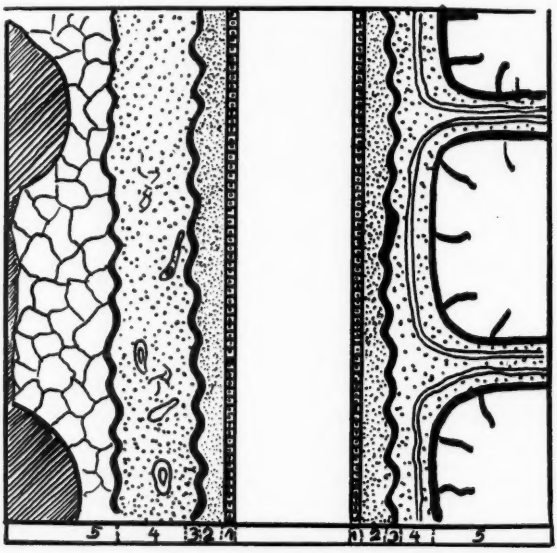

Fig. 1.—Structure of Pleural Layers. *1.* Mesothelium. *2.* Submesothelial avascular layer of connective tissue. *3.* Internal lamina elastica. *4.* Subpleural tissue. *5.* Deep layers.

epithelial surfaces of the peritoneum and pericardium, they represent the mesoderm and are ontogenically antecedent to the formation of the mesenchyme which is thought to play such an important role in inflammatory processes. When the lateral mesoderm gives rise to the embryonal celom, it forms the somatic and splanchopleural epithelia which remain as such throughout life and preserve all of its original potentialities, requiring the stimulus of the proper "evocative" for those potentialities to become manifest. This mesothelium—mesoderm functioning as epithelium—which even in fetal life, once morphologically formed, differentiates itself in some places into the gonadal blastoma (Gruenwald[7]), gives rise to the mesenchyme and plays an important part in the organization of adhesions, as was shown by Monckeberg[8] nearly fifty years ago. It is interesting that the mesothelial nutrition depends

upon imbibition through the submesothelial layer. The integrity of the mesothelium is entirely necessary for the free movement of the pleural leaves upon each other. Any interference with the subpleural circulation brings about the destruction of the mesothelium, and consequently leads to an adhesive process.

Fig. 2.—Visceral pleura of dog, twenty-four hours after the aggression. *a.* Fibrin. *b.* Serous fluid. *c.* Mesothelium separating from underlying layer. *d.* Mesothelium in hyperplasia. (Stained with alum hematoxylin and eosin × 200.)

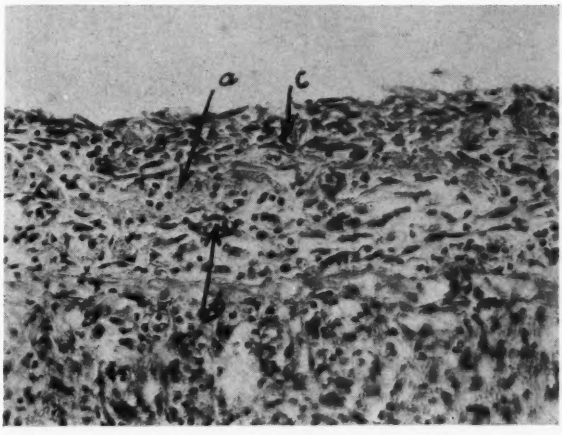

Fig. 3.—Visceral pleura of dog five days after the aggression. *a.* Remains of fibrin. *b.* Newly formed vessels. *c.* Proliferation of fibroblastoid elements. (Stained with alum hematoxylin and eosin × 200.)

Finally, attention must be drawn to the fact that a functional difference arises from the anatomic difference described. By means of the endothoracic fascia the parietal pleura is able to move independently of the deep layers, whereas the visceral pleura, due to its continuity with the lung through the

interlobular bands, presents regions which do not move. Therefore, during inspiration the bands protrude less than the lobules, and during expiration they protrude more. Thus, during breathing the pleura covering the pulmonary lobules moves more than that which is in contact with the bands, causing an uneven movement of the visceral pleura.

The diaphragmatic pleura, although it has no real basal fascia, behaves like the rest of the parietal pleura. As its relation to the diaphragm is limited to the lining it retains its unity of movement.

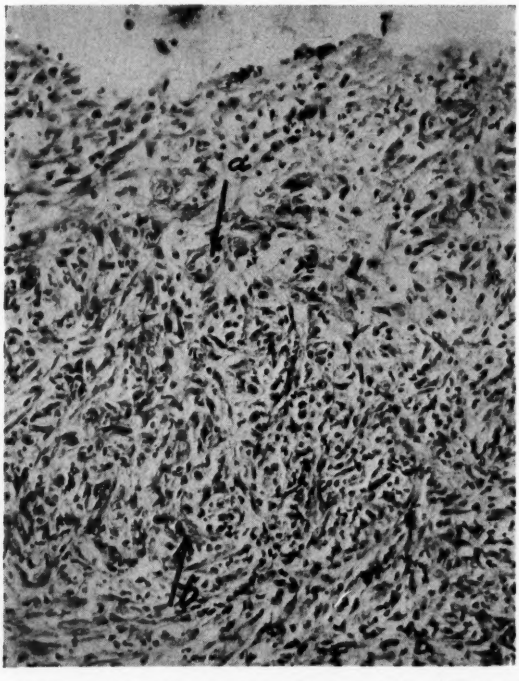

Fig. 4.—Visceral pleura of the dog ten days after aggression. Marked pleural thickening. Scarce remnants of fibrin. Predominant angiogenesis. *a.* Newly formed blood vessel, young structure. *b.* Exaggerated proliferation of fibroblastoid elements. (Stained with alum hematoxylin and eosin × 200.)

THE ORGANIZATION OF ADHESIONS

The majority of authors who have studied this subject, Steele,[9] Hanrahan,[10] Singer,[11] Ferretti,[12] Mistal,[13] and Castello,[14] and particularly "pleurodesis" or the formation of pleural adhesions as a therapeutic measure, cause the formation of adhesions by placing irritating substances in the pleural cavity. In our experience we caused minimal trauma without the use of any foreign substances, and our results were similar, on the whole, to those obtained by the authors mentioned above.

There are three successive stages in the formation of adhesions which do not differ from those present in the formation of granulation tissue. The first stage is fibrogenesis as a direct result of the intervention. The second is the stage of antigenesis, and the third is the stage of fibrogenesis. Twenty-four hours after the operation the mesothelium is destroyed and plasmatic material

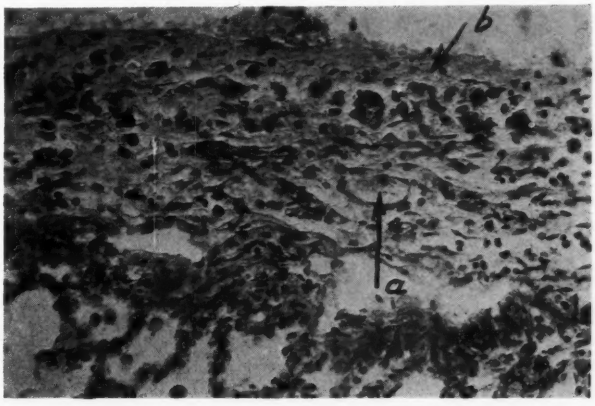

Fig. 5.—Visceral pleura of dog fifteen days after the aggression. *a*. Newly formed vessel. Deeply stained nuclei. *b*. Fibrogenesis commencing. (Stained with alum hematoxylin and eosin × 200.)

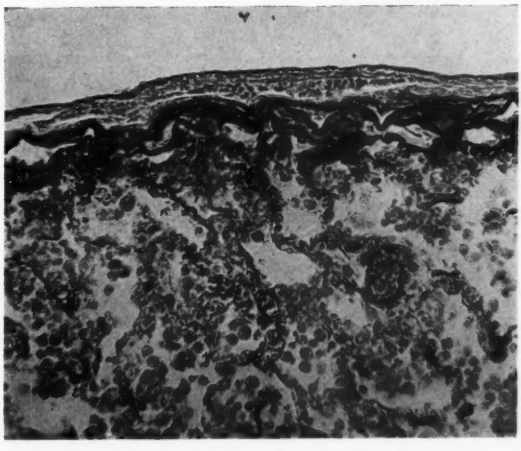

Fig. 6.—Visceral pleura of normal dog. (Stained with alum hematoxylin and eosin × 200.)

appears which on one side unites the mesothelial cells of the borders of the destroyed area, and on the other unites the edematous submesothelial tissue (Fig. 2). The stimulus for cell division is thus established, and the period of angiogenesis is reached. Here a large quantity of fibroblastoid elements appear whose only function seems to be the formation of blood vessels. (Figs.

3, 4, 5.) In the fibrogenetic period the mesothelial cells are transformed into mesenchymal elements and phagocyte the fibrin. In from ten to fourteen days the fibrin disappears almost completely, increasing the thickness of the pleura by edema, and cellular elements which are mainly angioblasts (Compare Figs. 3, 4, and 5 with Fig. 6 which shows a normal pleura). A large number of vessels are formed, of which, after fifteen days, only those which have become

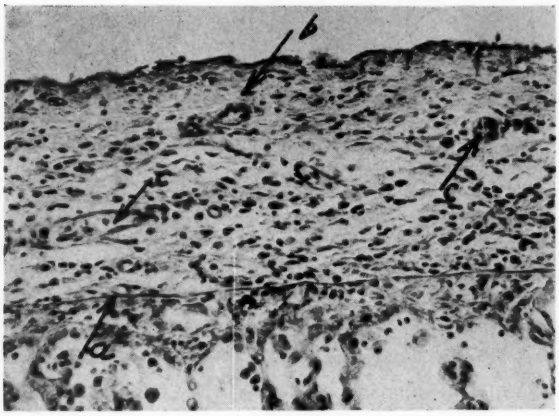

Fig. 7.—Visceral pleura of dog twenty days after the aggression. *a*. Internal elastica. *b*. Fibrosis of the superficial zone. *c*. Fully formed blood vessels. (Alum hematoxylin and eosin ×200.)

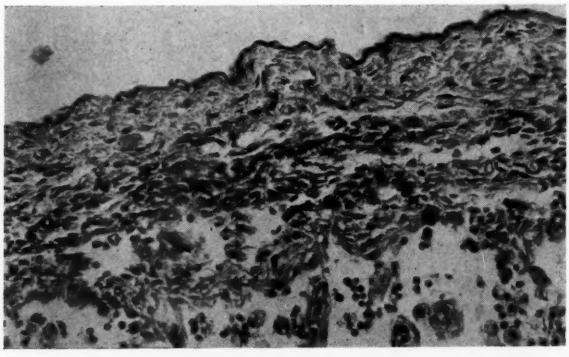

Fig. 8.—Visceral pleura of the dog thirty days after the aggression. Pleura thickened by total fibrosis. Here there are few cellular elements which are lengthened, have hyperchromatic nuclei, and there is much collagen between them. (Stained with alum hematoxylin and eosin × 200.)

true veins or arteries remain, while those in which the internal pressure is below that of the surrounding tissues become obliterated, and the angioblasts then form part of the sclerotic tissue as fibroblasts. After this period the stage of fibrogenesis is reached at about the tenth day. Fibrosis starts in the superficial areas (Fig. 7) later extending towards the deeper layers (Fig. 8). In

our material established fibrosis was found in a total of thirty days. The underlying structures remain intact (Fig. 9). A notable fact is that once the process of sclerosis has finished, the few cellular elements may become reactivated and proliferate actively when confronted with an adequate stimulus.

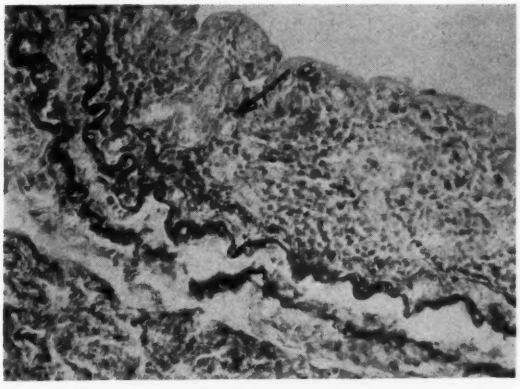

Fig. 9.—Visceral pleura of dog thirty days after the aggression. Observe the well-preserved laminae elasticae below the fibrosis. *a.* Newly formed blood vessel. (Stained with alum alum hematoxylin and eosin ×200.)

Fig. 10.—Visceral pleura of dog two months after the first aggression and twenty-four hours after the second. Established fibrosis. *a.* fibrin. *b.* proliferation of young fibroblastoid elements. (Stained with alum hematoxylin and eosin × 200.)

This may be observed in Fig. 10, where a consolidated adhesion (after two months) was stimulated by surgery, and twenty-four hours later fibrin is visible, and beneath it proliferation of the cellular elements which formed the established fibrosis. This proves that even after differentiation, and acquiring a stage which seems final, the mesothelial elements may become undifferentiated.

The most notable histologic fact is the speed of cellular division which usually takes place by amitosis. At present it is difficult to say what stimulus incites division. Harvey[15] believes that the products resulting from cellular destruction may act as "evocative" factors upon the mesenchymal cells and induce them to proliferate and differentiate into the various elements which constitute granulation tissue. We believe that fibrin must play a special inductive role, having observed that its presence in any area, especially on the mesothelium and vascular endothelium, activates proliferation very rapidly, as is not the case with any other substance.

Summarizing, we may say that there is first an inductive period which lasts for some hours, then a period in which the formation of vessels predominates and lasts up to fifteen days, and then a period of constitution, of fibrosis, which is complete in ten more days. The whole process lasts about thirty days. In the third period most of the vessels disappear, and only a few, which become arteriolized, remain and occasionally acquire the size of a peripheral artery.

PLEURAL REACTIONS TO AGGRESSION

The response of the pleura is different according to whether the aggression comes from the lung, or from the pleural cavity. The former are called internal aggressions, the latter external aggressions.

In the same way an internal aggression will have a different result if it is mechanical, or inflammatory. It has already been stated that the pleural mesothelium is a factor of foremost importance in the separation of the pleural leaves, and that its nutrition is maintained by imbibition through the submesothelial tissue. Any obstacle to the circulation brings about the separation of the mesothelium. Therefore, an inflammatory pleural lesion is not indispensable for an adhesion to form. This is in opposition to what has been upheld by many authors up to the present time. Smith[16] recently stated that, "inflammation is the basic cause of pleural adhesions," and although infarcts of the lung may have overlying adhesions, it is probably the inflammation of the pleura over the infarct which is the causal factor. Benign or malignant tumors, hydatid cysts, or even localized inflammatory lesions in the vicinity of the pleura obstruct the interlobular bands and, without invasion of the pleura, cause the mesothelium in the immediate neighborhood to become separated, due to the impossibility of exchange of oxygen and carbon dioxide because of the impaired circulation in the region. A surface which is unable to slide freely upon the other thus remains. The mesothelium of the parietal pleura becomes "evoked" and a "mechanical adhesion" is formed which, as is commonly seen by thoracic surgeons, marks the limits of the pulmonary lesion very accurately. In these cases where there is no inflammatory lesion, mesothelium neighboring the visceral pleura proliferates over the adhesion, covering it, and forming papillary protrusions (Fig. 11). These adhesions do not alter the superficial lamina elastica, and their freeing does not bring alterations.

The induration which follows an inflammatory process is caused by the progression of the lesion towards the vicinity of the mesothelium, which separates and an adhesion is formed. The organizing element of this adhesion originates in the parietal pleura, as is the case in a "mechanical adhesion," but in these cases the adhesive process extends past the limits of the

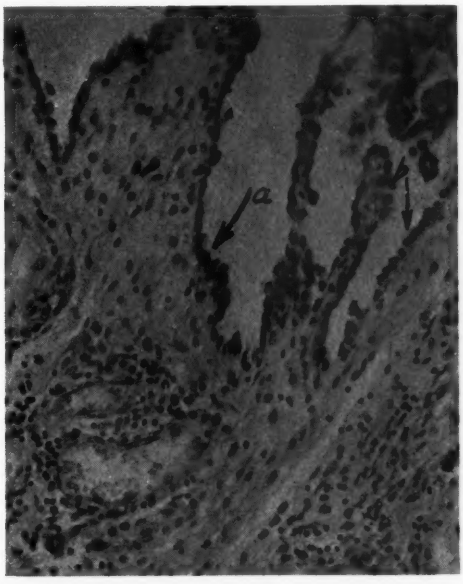

Fig. 11.—Visceral pleura near a pulmonary carcinoma. Observe the papillae covered with mesothelium. *a.* and *b.* Hyperplastic mesothelium. (Stained with alum hematoxylin and eosin × 300.)

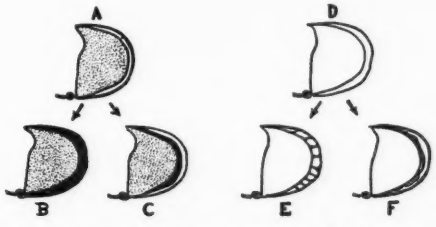

Fig. 12.—Diagrammatic sketch of transverse section of a hemothorax. *A.* Diseased lung with external aggression leads to *B*, total symphysis if the pleural space disappears; and to *C.* pachypleuritis if the cavity persists. *D.* Normal lung with external aggression leads to *E.* partial adhesions if the pleural cavity disappears and to *F.* visceral pleural shell or peel, and parietal pachypleuritis, if it persists.

lung lesion and the lamina elastica is partially destroyed. This is of importance because as a result of this the freeing of the adhesion may cause the formation of subpleural emphysema. This would also explain the pathogenesis of subpleural vesicles which appear in the zone of the visceral insertion of many of the adhesions, and which are observed at times during pleuroscopy.

In cases in which the aggression is external the result is determined by the condition of the lung, quality of the intrapleural material, and the preservation or not of the pleural space as a real cavity. In Fig. 12 one may see the results of an external aggression according to the different conditions prevailing. If the lung is diseased and the cavity disappears the final result will be an intimate adhesion between the two leaves, a pleural symphysis. This is seen in pulmonary tuberculosis treated by pneumothorax which is followed by a pleural effusion. In a limited form, it may be observed near tuberculous cavities (Fig. 13). If the lung is diseased and the cavity persists the result will be a thickening of the visceral pleura, a pachypleuritis. This may frequently be seen in patients receiving pneumothorax therapy for tuberculosis.

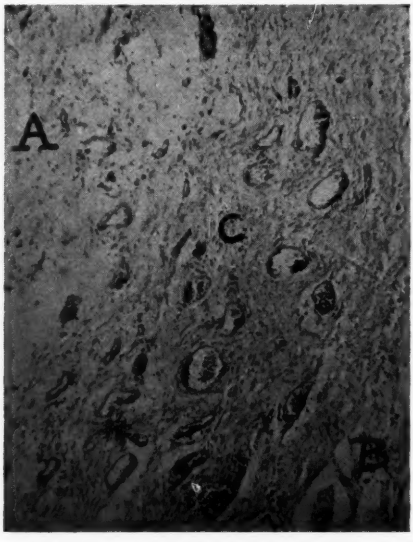

Fig. 13.—Total symphysis in case of pulmonary tuberculosis. *A*. Deep parietal zone. *B*. Deep visceral zone. *C*. Zone of symphysis with marked vascularization. (Stained with alum hematoxylin and eosin × 130.)

This response when the lung is diseased finds an explanation in that the mesothelium has a low vitality and any aggression, however slight, brings about its destruction. In these cases the pleural sclerosis also occurs in the interlobular septa, and many scleroses considered of pleural origin are due to this mechanism. Sometimes when the aggression is external, the lung collaborates in the formation of the pachypleuritis. In Fig. 15 an interlobular band is seen with circulatory alterations causing profuse edema. If one considers that the interlobular septa are just an intrapulmonary continuation of the pleural tissue, it may easily be understood that in cases of external aggression with a diseased lung this latter factor is very important in the formation of pachypleuritis. When the lung is healthy and the pleural cavity dis-

appears, the result will be the formation of partial adhesions. This is what happens in cases of serofibrinous pleurisy of short duration, or in minor hemorrhagic pleural effusions of traumatic origin.

When the lung is normal and the pleural cavity persists, and aggression takes place, a pleural shell or peel is formed, instead of pachypleuritis. Some

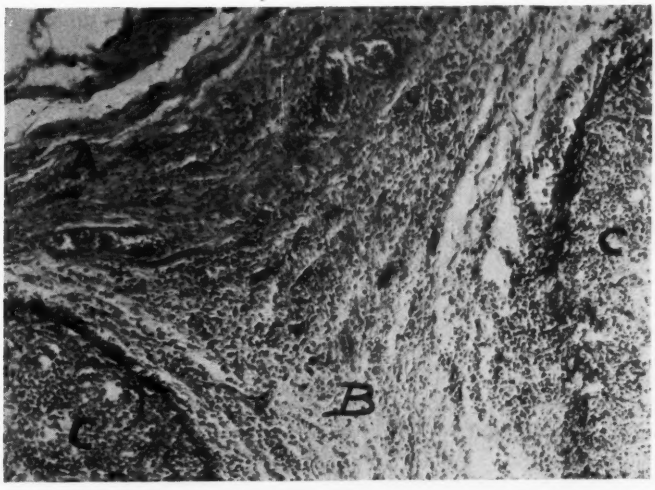

Fig. 14.—Inflammatory process of the pleura (*A*) continuing in the interlobular septa (*B*). *C*. Lung. (Stained with alum hematoxylin and orceine × 200.)

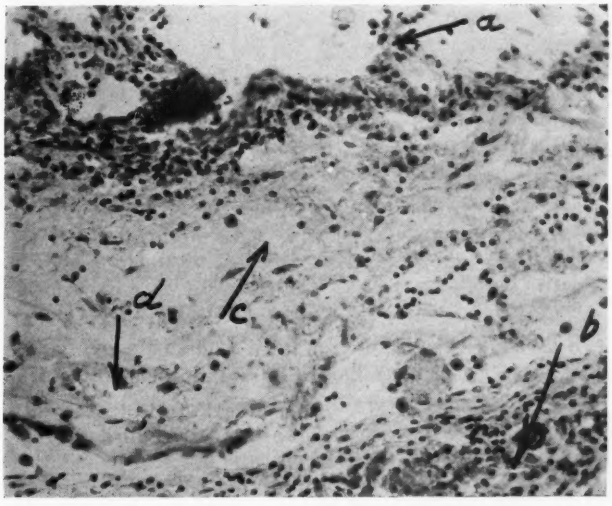

Fig. 15.—Interlobular septa in a case of pulmonary tuberculosis. *a*. Interalveolar septa. *b*. process of pulmonary condensation. *c*. marked edema. *d*. vascular dilatation. (Stained with alum hematoxylin and eosin × 200.)

authors erroneously call this a pachypleuritis. It may be observed in cases of chronic empyema of short duration, traumatic hemothorax, and in therapeutic pneumothorax. The most notable macroscopic characteristic is the existence of a lardaceous membrane which adheres to the visceral pleura, but from which it may be easily separated, leaving the visceral pleura absolutely normal as to its smooth surface, sheen, and transparency. This lardaceous membrane also exists on the parietal pleura, but it is much more adherent to it, only being separated from the deeper layers by the cleavage plane formed by the endothoracic fascia. Once it is detached, the parietal pleura which comes away with it does not retain its normal features and therefore cannot be considered as a pleural peel but as a state of pachypleuritis. Those who have studied the subject have not considered the marked difference between

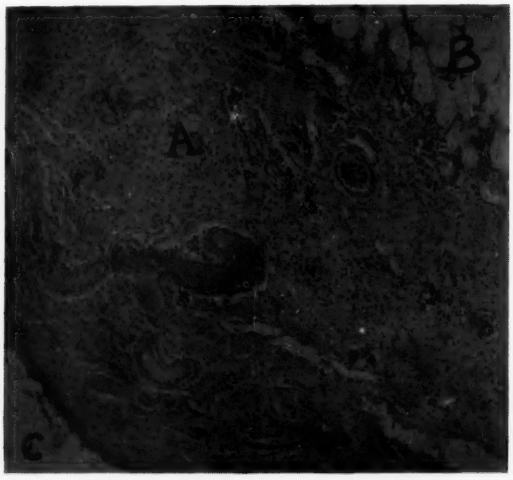

Fig. 16.—Specimen of pulmonary decortication. *A*. Parietal pleura. *B*. Segment of fascia. *C*. Superficial zone. (Stained with alum hematoxylin and eosin ×130.)

the response of each pleura and speak of a pleural peel for both the parietal and visceral pleura. Klopstock[17] has recently stated that the parietal peel adheres to, but does not involve, the pleura. Langston and Tuttle[18] have spoken similarly in a paper on the pathology of chronic hemothorax. This error which delays the correct knowledge of the pathogenesis of the pleural peel is due to the fact that those who have studied the subject are surgeons, and they have not examined histologically the fibrous material which has been removed. They have failed to see that what was separated along the cleavage plane of the endothoracic fascia was the thickened pleura. We have found the same fact on histological examination: the parietal pleura thickens evenly and extends in depth as far as the fascia (Fig. 16) while the visceral fibrous membrane adheres to the pleura only by small areas of union (Fig. 17). The thickening of the parietal pleura is always three or four times greater

than the thickness of the visceral lardaceous membrane. The process, in the form of pachypleuritis and peel, extends to the entire pleura, and the lung is incarcerated and unable to expand. Surgical treatment, first performed fifty-five years ago by Delorme, frees the lung and allows it to recover its original functional capacity in most cases. If this functional recovery is not always as complete as may be expected, it is in part due to the removal of the thickened parietal pleura which leaves a raw surface which does not correspond to the smooth surface of a serosa but to a more or less lax connective tissue. The reexpanded lung thus becomes adherent to the chest wall and this interferes with normal breathing function. The removal of the thickened parietal pleura has, on the other hand, two favorable consequences as a result of the formation of the adhesion. These are to increase the elasticity of the chest wall and to insure the fixation of the lung in full expansion when the decortication has been done for a chronic pneumothorax.

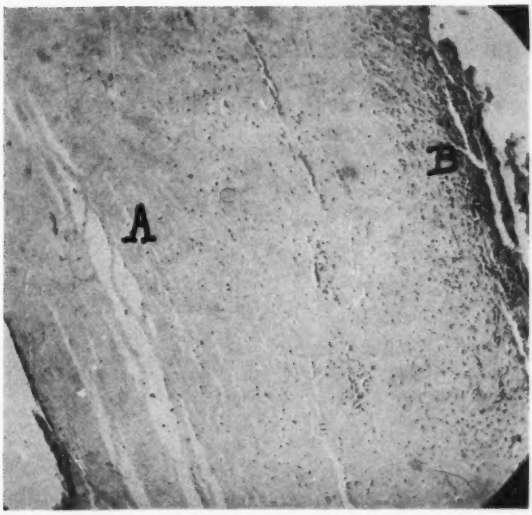

Fig. 17.—Hyalininized pleural shell removed at operation. *A*. Superficial zone. *B*. Deep zone. (Stained with alum hematoxylin and eosin ×130.)

The problem to be faced is why a pachypleuritis involves the parietal pleura and not the visceral, and how the material in contact with the visceral pleura becomes organized without the pleuras being altered macroscopically. Both problems are related to the differences, both anatomical and functional, between the two pleural leaves which have been previously described. In cases of chronic hemothorax, or other processes which lead to the formation of a pleural shell, or peel, the material coagulates and the fibrin adheres to the parietal pleura, causing an intimate contact which causes the mesothelium to be stimulated or to separate, leading to the organization of the material

by the same mechanism as in the formation of adhesions. In the visceral pleura, when the lung is normal, the mesothelium remains whole except where the contact between the fibrin and the mesothelium is most intimate. This area corresponds to the part of the visceral pleura which moves the least,

Fig. 18.—Peel formation in a case of recent pleural effusion. *a.* fibrin. *b.* union starting at level of the septa. *c.* preserved mesothelium. (Stained with alum hematoxylin and eosin × 130.)

Fig. 19.—Peel formation. Higher magnification of field in Fig. 18. *A.* Fibrin. *B.* Septa. *a, b,* and *c,* mesothelial cells. Notice intimacy of adhesion between the septa and the fibrin. (Stained with alum hematoxylin and eosin ×300.)

where it covers the interlobular bands, and it is there where organization occurs (Figs. 18 and 19). The process of organization does not differ from that which may be seen in other parts, but the source of the organizing material is at the level of the interlobular bands. The mesothelium proliferates and covers the inferior part of the organized membrane, following as points

of reflection the unions at the level of the interlobular bands. In cases of chronic empyema the material is more traumatic, and with time the septa are overrun, and a simple, visceral, pachypleuritis develops.

SUMMARY AND CONCLUSIONS

1. The visceral and parietal pleura, due to their different anatomic structure, react in a different manner to aggression.

2. An adhesion is completely formed in thirty days, going through three periods: one of evocation of the mesothelium, another angiogenic, and a third fibrogenic. The mesothelium has a preponderant role in the organization of the adhesion.

3. The adhesions following a noninflammatory pulmonary lesion are mechanical adhesions, and the visceral lamina elastica is not altered. In the adhesions caused by an inflammatory process which affects the pleura (inflammatory adhesions), the lamina elastica is not spared, and pleuroscopy may reveal vesicles of subpleural emphysema.

4. External pulmonary aggression causes pachypleuritis when the lung is diseased and there is a true pleural space. It causes symphysis when the lung is diseased and the pleural cavity disappears. It produces a pleural shell or peel when the lung is healthy and the cavity persists.

5. The parietal pleura never forms a shell but it becomes thickened as the result of a pachypleuritis. A shell should form on the visceral pleura when the lung is healthy, and the pleural cavity persists when there is external aggression.

6. The organization of the material in contact with the visceral pleura starts in the mesothelium which covers the interlobular septa, because at that level the pleura moves less during respiration than at the level of the lobules, allowing a more intimate contact between the intrapleural material and the mesothelium.

7. In the act of decorticating the lung, the surgeon removes the shell leaving the visceral pleura more or less intact. In removing the thickened parietal pleura, the site of pachypleuritis, he does so along the plane of the endothoracic fascia.

The authors wish to express their gratitude to Dr. Oscar A. Vaccarezza for his valuable suggestions and the many specimens he put at their disposal.

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THE USE OF STREPTOKINASE-STREPTODORNASE IN THE TREATMENT OF POSTPNEUMONIC EMPYEMA

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AMONG patients with various types of subacute and chronic suppurative diseases that have been treated with streptococcal concentrates containing streptokinase and streptodornase (also referred to as SK-SD), cases of empyema constitute a group in which the indications for enzymatic therapy have often been well defined in accordance with the principles that have been developed for their use, and the results have often been unusually favorable.

Previous reports have dealt with the range of successful and possible clinical usages of the streptococcal enzymes for therapeusis,[1, 2] and the development of the study from its inception has been reviewed.[3] In separate articles[4] studies dealing specifically with hemothorax have been recently presented.

In is the purpose of this article to record the results of our investigations and clinical experiences in the treatment of cases of empyema in which the suppurative pleurisy developed specifically as a complication of acute pneumonia. Twenty-five cases comprise the postpneumonic group.

Twenty-one of the patients were treated without recourse to operative procedures. In four instances, solutions of SK-SD were employed in association with closed thoracotomy.

Other types of empyema which have also been studied in relation to SK-SD therapy have consisted of patients with protracted chronic suppurative diseases, often with draining sinuses, and usually of many months' or even years' duration. This latter group has included diverse types, both with and without previous operative procedures, that differed widely both with respect to etiologies and bacterial contaminations, and also to the underlying thoracic diseases on which the local persisting infections were superimposed. The problems have accordingly varied over a wide range both bacteriologically and pathologically. The results of the special studies which they have required will be given in a separate communication.

MATERIALS AND METHODS

In connection with the specific action of the enzymes, it is important to recognize the fact that both streptokinase and streptodornase are necessary in cases of purulent infection, since both fibrin and particularly desoxyribose nucleoprotein make up the greatest proportion of the solid sediment of purulent exudates. As described in detail in the previous article,[4b] SK alone is of prime significance in the massive extravascular coagulum of hemothorax. However,

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the action of streptodornase assumes special importance where exudation of infectional origin is present. The details of the action of SD, both in vitro, and in vivo in patients, have been described.[5]

The contents of sterilized, lyophilized ampules containing mixtures of streptokinase (SK) and streptodornase (SD) in powdered form* have been put in solution in sterile physiologic saline. The material has then been injected or instilled promptly into the pleural area since deterioration of the enzymes occurs rapidly at either room or the usual icebox temperatures, after the solution has been made.

Dosage: A mixture of approximately 200,000 units of SK and 60,000 units of SD in 20 c.c. of solution has proved satisfactory for single intrapleural injections. All of the lots of SK-SD available for therapeutic trial have not uniformly had the ratio of 3 to 4 units of SK to 1 unit of SD indicated above. However, within the range of 100,000 to 250,000 units of SK plus 50,000 to 125,000 units of SD, effective results have been obtained without undue toxicity.

In general, the dosage has borne a relation to the size of the area of disease into which the solution was introduced. In intrathoracic diseases, relatively small areas have been encountered in patients of the pediatric age group and in adults with residual pockets of restricted size. In the latter instances it has been our practice to prepare a solution containing approximately 10,000 units SK, 4,000 units SD per c.c., and introduce as much as will be conveniently retained.

Laboratory Methods of Determining Enzymatic Action.—

It is unnecessary to recapitulate the biochemical, biophysical, and histological-cytological methods that have been employed in measuring the action of the enzymes.[1, 5, 6]

The three most practical procedures of estimating whether or not enzymatic alterations of purulent exudates have occurred are:

1. Grossly visible changes in the character of samples of fluid removed within twenty-four hours of the introduction of SK-SD.

2. Determinations of the amount of sediment in centrifuged specimens of equal quantities of exudate derived from specimens taken before, during, and after treatment.

3. Microscopical examinations of specimens stained by the Feulgen method which is histochemically specific for desoxyribose nucleoprotein.

Fig. 1 is an example of the effect of SK-SD on the gross appearance of thick purulent material. The extensive lysis with thinning of the exudate was apparent by gross inspection at the time of the first posttreatment aspiration.

Although in most of the cases, the pretreatment specimens of exudate had the classical thick, coarsely granular appearance of pus, some of them have been found by detailed examination to vary with respect to viscosity, cloudiness, and degree of sedimentation. In this connection the interesting observation has not infrequently been made that thin, even serous, pretreatment specimens have

*Supplied by Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

become grossly purulent within twenty-four hours following the injection of SK-SD. The factors responsible for this apparent paradoxical type of change will be discussed in connection with the patients in whom the observations were made. However, Fig. 2 gives a specific illustration of this type of finding.

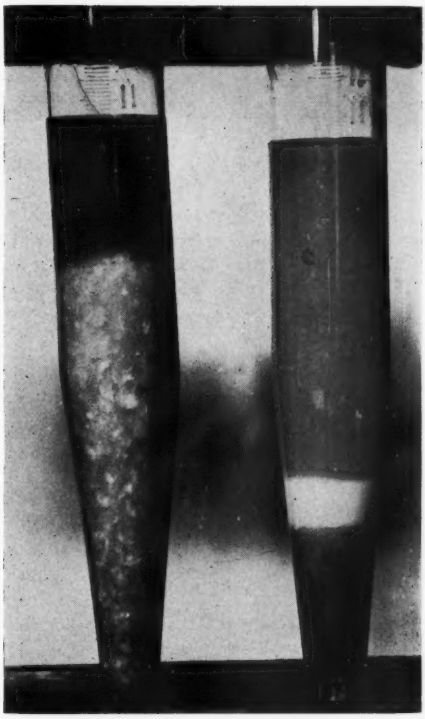


Fig. 1.—Rapid lysis by SK-SD of purulent pleural exudate within pleural cavity of patient. (Chronic pulmonary tuberculosis, left bronchopleural fistula, pyopneumothorax, and thoracotomy.) *Specimen at left:* Taken immediately prior to injection. Ten cubic centimeters centrifuged for one hour. Sediment: 70 per cent—thick, pink, viscid, and containing large shreds. Viscosity of whole fluid 150 times water. *Specimen at right*: Removed from chest one hour after injection. Ten cubic centimeters centrifuged for one hour. Sediment: 23 per cent—separated readily into three layers. From bottom up: small viscid layer, large pink layer of mixed red and white blood cells; and white layer composed of white cells and granules. Viscosity of whole fluid 4 times water. (Reprinted from J. Clin. Investigation 28: 184, 1949, with permission of the Editors.)

An example of the third laboratory method of determining the enzymatic action as seen in microscopical examinations of preparations stained by the Feulgen method is given in Fig. 3. The disappearance of the abundant extracellular nucleoprotein is readily demonstrable. The details of the technique employed by us are given in reference No. 5.

Practical Management of Cases of Closed Empyema.—

The selection of the most appropriate site or sites for the instillation, as determined by roentgenograms and fluoroscopy, has been considered of special importance since maximum liquefaction requires direct contact between enzymes and substrates.

The enzymatic solution, usually 20 c.c. in amount, has been introduced intrapleurally after the removal of as much exudate as may be aspirated with relative ease.

The first posttreatment aspiration has been performed twelve to eighteen hours after the injection. The thoroughness and completeness of this thoracentesis is considered to be of special importance, since it (a) fulfills the prime objective of the therapeutic measure—namely, the removal of the pus, (b)

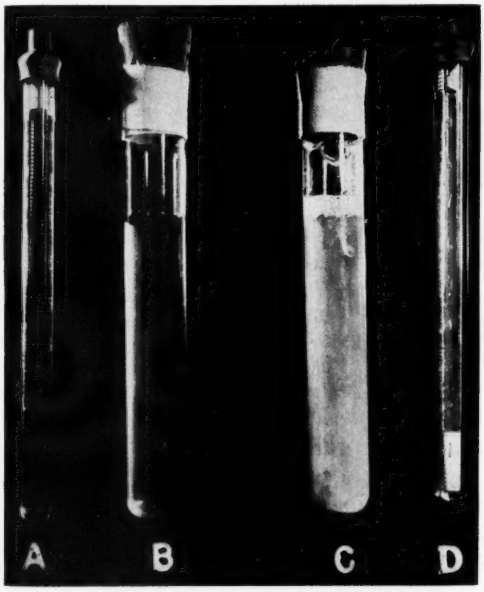


Fig. 2.—Liberation of purulent exudate by intrapleural action of SK-SD in patient with postpneumonic loculated empyema, sterile (Case D. L.—see text). Tubes A and B on left contain specimens removed just prior to injection of SK-SD. *A.* Wintrobe sedimentation tube centrifuged for one hour at 2,500 RPM. Sediment 1 per cent. *B.* Test tube shows fluid (uncentrifuged) of a slightly cloudy serous character. Tubes C and D on right contain specimens removed twenty-four hours after SK-SD. *C.* Test tube shows fluid of low viscosity (uncentrifuged) but grossly purulent in character. *D.* Wintrobe sedimentation tube centrifuged for one hour at 2,500 RPM. Sediment 14 per cent.

permits the evaluation of the degree of pulmonary expansion, (c) removes residual toxic materials, and (d) affords the opportunity of fresh locally appearing leucocytes, serum, and antibiotics to make contact with the offending bacteria.

In some instances when the configuration of loculations has been conspicuously evident before treatment, fluid levels have been observed by fluoroscopic examinations made early after the injections to disappear after a few hours of enzymatic dissolution.

Subsequent aspirations have usually been performed as indicated followed by frequent x-ray examinations to estimate changes in pleural densities.

Additional injections have been employed when, after two to four days, appreciable amounts of residual deposits were noted, or bacteriological cultures

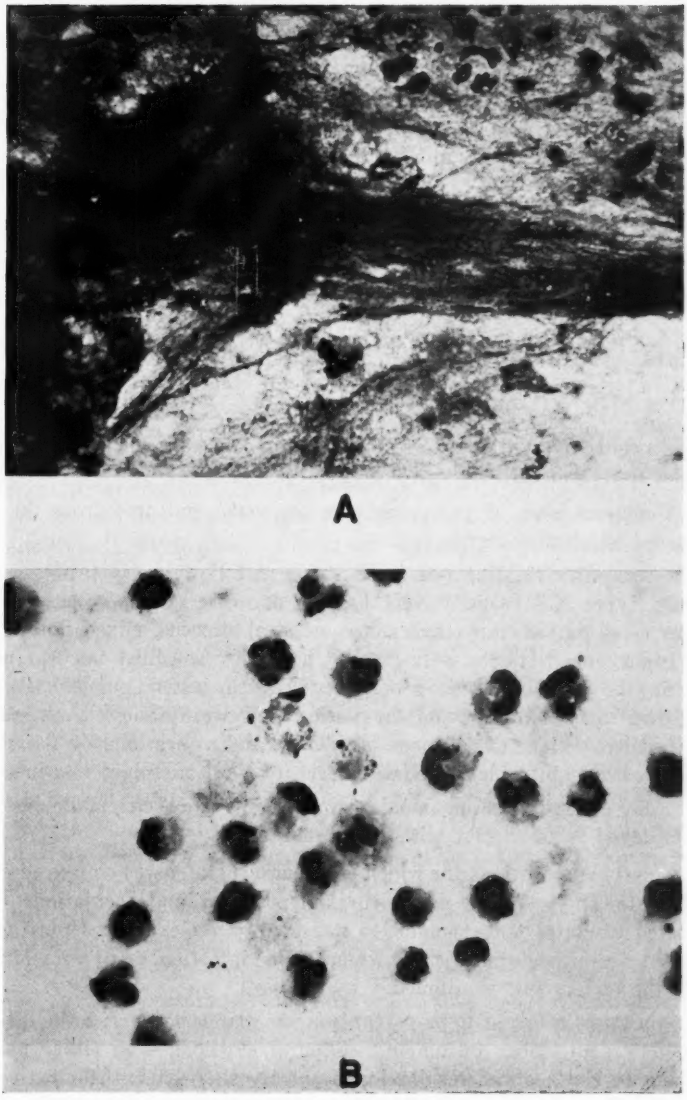


Fig. 3.—*A*. Feulgen stain of pleural exudate aspirated from a patient with a thick tuberculous empyema, immediately before the local injection of SK-SD. The nuclei of the luecocytes and extensive extracellular amorphous plaques and fibrous strands take the Feulgen stain ×882. *B*. Feulgen stain of pleural exudate aspirated from Case N. M., two hours after the local injection of SK-SD. The extracellular matrix has been swept clean of the Feulgen staining material ×882. (Reprinted from J. Clin. Investigation 28:1094, 1949, with permission of the Editors.)

remained positive. As will be noted in the subsequent case reports, longer intervals between injections have occurred when residual active infection or exacerbations served to indicate the desirability of additional treatment.

Multiple injections, simultaneously administered into two or three different sites, have been employed when only a few cubic centimeters of exudate could be obtained by aspiration from multiple areas, yet the roentgenogram depicted an extensive density. Under these circumstances the dosage of multiple injections has been that of one to two therapeutic doses, divided into aliquot parts.

The transient pyrogenic reactions which may follow the injection have been previously referred to,[1] and the total toxic reactions, none of which have proved to be serious, have been described in detail.[3] The administration of amidopyrine (0.6 Gm. four times a day) on the day preceding and the day of treatment has abolished the thermal reaction and abated considerably the symptoms. Aspirin has proved useful, but less effective than amidopyrine.

CLINICAL RESULTS

The twenty-five patients have been divided into three groups as recorded in Tables I, II, and III. They are as follows:

1. Fourteen cases of postpneumonic empyema, cultures from the pleural exudates of which were sterile.

2. Seven cases yielding positive cultures as follows: (a) two cases (Pneumococcus Types XXII and XXXIII), (b) one case (*Streptococcus viridans*), (c) four cases putrid empyema (anaerobic streptococcus, mixed flora, *E. coli*). These twenty-one patients were treated solely by so-called medical measures which, in the postpneumonic group, began with systemic antibiotic therapy during the early acute pneumonic period and were followed ultimately by intrapleural injections of solutions of SK-SD and aspirations by thoracentesis, with and without intrapleural administration of antimicrobial reagents.

3. Four cases of postpneumonic empyema in which enzymatic instillations were employed in association with closed thoracotomy.

The specific conditions for which enzymatic therapy was employed consisted of either the presence of intrapleural depositions and loculations of thick inspissated exudates not amenable to satisfactory removal by aspiration, or to the persistence of bacteriologically demonstrable infection, or to a combination of both of the factors just mentioned.

In the cases referred to as *postpneumonic empyema, sterile* the disease was initiated by acute lobar pneumonia. Pleural effusions were either present on admission to the hospital or developed shortly thereafter. The patients were usually considered to be seriously ill at the beginning and type specific pneumococci were in most instances demonstrated in sputum or blood culture. Protracted and intensive penicillin therapy was continued beyond the early acute phase because of the persistence of fever and leucocytosis together with the physical findings of pneumonia and pleural effusion.

When the diagnosis of empyema was first made specimens of the pleural exudate were usually grossly purulent in character, although in some instances

the effusion appeared cloudy with skeins of fibrin present, and in a few, clear serous material was aspirated.

Cultures were uniformly sterile, presumably due to the intensive penicillin therapy. Otherwise the disease resembled pneumococcal empyema from which, in nontreated cases, type specific pneumococci are regularly recovered.

Aspiration by thoracentesis became increasingly unsatisfactory as the disease progressed, and roentgenograms exhibited the characteristic gross shadow of pleural effusion often with demonstrable loculations.

Intrapleural instillation of solutions of SK-SD were given during the first to fourth weeks of hospitalization usually at a time when the clinical condition had either reached a static state characterized by varying degrees of general sepsis, or the rate of improvement was so retarded that it seemed desirable to intervene with appropriate local therapy in order to hasten final clearing.

Data referable to the treatment in the first fourteen patients are given in Table I.

The findings recorded in Table I may be divided into the following essential categories: (1.) The effect of SK-SD on the exudate itself as manifested by (*a*) the successful evacuation of increased quantities of fluid resulting from the lytic enzymatic action, and (*b*) the concomitant changes in the characteristics of the specimens that reflect the physical alterations described under Materials and Methods. (2.) The extent and nature of the immediate direct effects of SK-SD on the general clinical state as well as the local pleural disease. (3.) The ultimate results with respect to final clearing.

COMMENTS ON THE COLUMNS OF TABLE I

The age of the patients varied from 33 to 92 years. In our total experience with the use of the streptococcal enzymes in patients of all age groups, including children, no differences in their specific actions or degrees of toxicity have been observed that were attributable to the factor of age.

With respect to sex, it is of interest briefly to note that twenty-two of the twenty-five patients listed in Tables I, II, and III were males. The preponderance of the occurrence of empyema among men has been previously mentioned.[7] No basis for this special finding is yet apparent.

The patients became available for injections of SK-SD over a relatively wide range—fifth to forty-second day—of estimated duration of disease. In this respect they were unselected, since an important part of the study has been directed toward determining the most favorable time in the course of the disease at which the enzymatic therapy may be most employed. Factors that are involved in this problem will be described in the subsequent discussions of the results.

Concerning the immediate and direct effects of SK-SD on the exudate itself, the significant increases in the quantity of fluid removed are evident from the data of Table I in adjacent columns. The large volumes were removed by aspiration with relative ease, which is accounted for both as a result of the thinning effect of the enzymes on the viscous coarse material and also on the fusion into a single area of previously noncommunicating loculated pockets. (See roentgenograms of patient D. L., Fig. 4.)

TABLE I. CASES OF POST-PNEUMONIC EMPYEMA (PRE-TREATMENT CULTURES STERILE)

PATIENT (NO.)	AGE (SEX)	EST. DURATION PRIOR TO SK-SD (DAYS)	EFFECT OF SK-SD ON EXUDATE		NO. INJ. SK-SD (DAYS)*	TOTAL FL. ASP. POST SK-SD (DAYS)†	EFFECT WITHIN 1ST 24 TO 48 HOURS, POST SK-SD		SUBSEQUENT COURSE ROENTGENOGRAMS	
			FL. JUST PRIOR TO SK-SD	FL. ASP. WITHIN 24 HRS. OF SK-SD			CLINICAL	X-RAY	DISCHARGED FROM HOSPITAL	FOLLOW-UP
T. P. (1)	40 (M)	19	c.c. 50 (Thick, purulent)	c.c. 465 (Thin, cloudy)	1	c.c. 465 (1)	Marked	Ext. Clearing	Small residual density	Clearing complete 6 months
E. K. (2)	33 (M)	19	5 (Serous, cloudy)	300 (Purulent)	1	400 (7)	Marked	Ext. Clearing	Clearing complete 4 weeks	
D. L. (3)	37 (M)	8	30 (Serous, cloudy)	400 (Purulent)	1	925 (5)	See Fig. 4		Clearing complete 4 weeks	Clearing complete 6 weeks
W. W. (4)	38 (M)	17	400 (Purulent)	800 (Thin, cloudy)	2 (20)	1620 (24)	See Fig. 5		Clearing complete 4 weeks	Small residual density 6 months
E. A.‡ (5)	40 (F)	25	15 (Purulent)	300 (Thin, cloudy)	1	300 (1)	Marked	Ext. Clearing	Clearing complete 4 weeks	Clearing complete 2 months
Mc. B. (6)	35 (M)	8	60 (Mod. purulent)	325 (Thin, cloudy)	2 (12)	1175 (15)	Definite	Ext. Clearing	Clearing complete 4 weeks	?
W. H. (7)	48 (M)	5	300 (Thin, cloudy)	300 (Thin, sanguineous)	2 (14)	1900 (17)	Definite	Reaccumulated Cleared after 2nd inj.	Small residual density	?

W. T. (8)	52 (M)	6	2 (Serous, clear)	700 (Thin, cloudy)	3 (27)	1900 (29)	Definite	Reaccumulated Cleared after 2nd and 3rd inj.	Small residual density	Clearing complete 2 months
F. D. (9)	39 (M)	5	650 (Sero-purulent)	700 (Less viscid)	2	3150	Definite	Ext. Clearing	Clearing complete 3 months	
J. S. (10)	48 (M)	26	250 (Mod. purulent)	250 (Thin, cloudy)	2 (3)	610 (11)	Definite	Mod. Clearing	Small residual density	?
N. R. (11)	64 (M)	22	40 (Thin, cloudy)	200 (Thin, cloudy)	2 (3)	1100 (7)	Gradual	Slight Clearing	Complicated by the presence of heart failure	
A. S. (12)	92 (F)	21	30 (Serous, clear)	300 (Thin, cloudy)	1	440 (7)	Gradual	Partial	Complicated by persistence of senile bronchopneumonia	
W. S. W. (13)	75 (M)	30	5 (Thick, purulent)	10 (Thin, cloudy)	2 (4)	190 (7)	Afebrile before inj.	Slight Total area small	Small residual density	?
J. B. (14)	66 (M)	42	20 (?)	50 (Thick, purulent)	3 (6)	215 (7)	Unchanged Afebrile before inj.	Unchanged	Open thoracotomy 15 days post-SK-SD. No exudate. Thick pleural wall present.	

All patients (except W. W. [4] received penicillin or other antibiotic during period of SK-SD therapy.
*Figures in parentheses indicate interval between injections when more than one was given.
†Figures in parentheses indicate number of days after 1st injection of SK-SD that aspirations by thoracentesis were performed.
‡Patient E. A. was treated at Hospital of Rockefeller Institute by Dr. E. D. Kilbourne.

An additional factor contributing to the quantity of fluid has been shown to be due to the local irritating effects of the enzymatic preparations which evoke an outpouring of fresh serum and leucocytes. This nonspecific reaction is of short duration but has appeared to be primarily responsible for small amounts of residual effusion that persisted for a few days after the initial successful removal of the major portion of liquefied exudate.

From a qualitative standpoint the gross appearance of the pretreatment specimens of exudate was usually a characteristic homogeneous pus. However, in some instances they varied from moderately cloudy to thin serous material. The factors which determine the gross appearance seemed to be referable to the extent to which the coarse and viscid elements were part of the free exudate or were deposited in solid form on the pleural surfaces leaving the overlying liquid portion relatively clear. Irrespective of the quality of the pretreatment exudates, thoracenteses had proved unsatisfactory in altering substantially the state of the empyema. Consequently, the problem of effectively evacuating the pleural contents was the same regardless of either the homogeneity or layered characteristics of the exudative material.

Patients E. K. (2) and D. L. (3) of Table I may be pointed out as examples of instances in which the empyema consisted essentially of exudative depositions on the pleural surfaces. Following injections of SK-SD the solid material was released by liquefaction with a resultant prompt change in the character of the fluid from serous to purulent. Subsequently the fluid became thin again as the pleuritis subsided.

The next column in Table I deals with the *number of injections* of SK-SD that were administered. As previously indicated, the dosages were approximately 200,000 units of SK plus 60,000 units of SD.

It may be noted that five of the patients received a single injection, seven received two, and in two instances, three treatments were given. Two of the patients, F. D. (9) and N. R. (11), received multiple injections given simultaneously into different sites in an effort to break up pocketed areas that did not appear to be directly contiguous.

The results obtained in the patients who received one treatment were both definite and prompt in promoting extensive evacuation of the empyemal pocket, in ameliorating rapidly the general clinical condition, and terminating the disease.

In the patients in whom a second injection was given within a week of the first, indications for the repetition of treatment were based on the presence of an appreciable amount of residual shadow after the response to the initial dosage and subsequent aspirations had been evaluated. The second treatment appeared to hasten substantially the final clearing which followed in the next three to four days.

In the cases in which the repetitions of injections were delayed twelve days or longer, the response to the first treatment was definitely favorable. However, because final clearing seemed, on clinical grounds, to be unduly protracted, an effort was made to abolish rapidly the remaining evidence of pleural involvement. The final response seemed effectual since subsequent reformations

of effusions were limited to a few days. However, up to the present time the requirements for repetitions of enzymatic therapy have not been amenable to uniform standardization because, once the relatively unsatisfactory state that served as a primary indication for the use of SK-SD had improved, the rate of clearing that may subsequently follow spontaneously has been subject to considerable variation. Consequently clinical judgment has, up to the present time, served as the chief guide in considering whether or not additional advantage may be gained by further enzymatic therapy.

An integral part of the subject just discussed concerns the period in the course of the empyema at which SK-SD may be most advantageously employed. Although there are exceptions to be noted in Table I, the cases treated relatively early after the development of empyema usually required additional treatments and aspirations. For example, patients Mc. B. (6), W. H. (7), and W. T. (8), of Table I received their first injections of SK-SD on the eighth, fifth, and sixth days after the detection of the presence of significant degrees of pleural exudation. In them, aspirations were performed intermittently over fifteen, seventeen, and twenty-nine days, and two or three enzymatic treatments were given. The evidence indicates that reaccumulations of the effusions may have occurred as a result of the continuation of active pleural or sub-pleural inflammation. Since the action of the enzymes ceases within the first twenty-four hours, the subsequent reformation of exudation appears to depend on whether or not underlying disease activity has persisted beyond the first evacuation of the pleural contents. When the reaccumulations have been sufficient to be of clinical significance, the injections of SK-SD given later were followed by a rapid termination of the disease. This subject is of special interest in connection with the course of the injections in the patients included in Table II, and will be further discussed. However, it seems possible that if the early treatment had been promptly repeated one or more times, final termination might have occurred in a shorter period of time.

In analyzing the clinical results, the injections of SK-SD have been considered to be effective in the first ten patients listed in Table I. In them, a decided improvement was evident within the first forty-eight hours. In some, fever and general symptomatology disappeared by crisis, and in others defervescence began promptly followed by continued improvement to complete recovery.

The first radiographic studies made, post SK-SD, have revealed the substantial changes brought about both in the density and in the configuration of the pleural shadows.

After all therapeutic procedures were stopped a thin residual density at the periphery of the lung and a partially flattened but mobile diaphragm were noted during the period of convalescence in the hospital. Total expansion was only slightly limited.

Final roentgenogram clearing was complete during the ensuing two to six months.

Patients N. R. (11) and A. S. (12), who responded well to enzymatic therapy, were of special interest. N. R. (11), aged 64 years, had congestive

heart failure which contributed to the pleural effusion and which served as a contraindication for the use of surgical measures in draining the empyema.

In patient A. S. (12) who was 92 years of age, the response to injections of SK-SD was prompt and definite, even though bronchopneumonia persisted on the basis of extreme senility.

In the last two patients listed in Table I, W. S. W. (13), and J. B. (14), no appreciable effect of the enzymes was demonstrable. It may be noted that they became available for injections of SK-SD after the empyema had been under observation for thirty and forty-two days, respectively. Studies indicated that cellular organization or other local changes in the tissues had occurred that were not subject to liquefaction by the streptococcal enzymes. That the effectiveness of SK-SD is conditioned by the chemical composition of the pathologic substrate with which they come in contact has been particularly emphasized,[3, 4b] and will be more extensive considered in our separate report dealing with chronic suppurative diseases of protracted duration.

It should be pointed out that in our total experience the occurrence of extensive permanent pleural organization in postpneumonic empyema of *pneumococcal* etiology is unusual. That slow spontaneous resolution may proceed to eventual clearing in pneumococcal empyema was reported earlier in association with the use of penicillin locally in such cases.[7] Consequently it seems likely that when extensive pleural organization and thickening occurs its development is referable to other special factors in the local disease processes that have not yet been identified.

In order to illustrate some of the types of responses to SK-SD just described, the protocols of two cases given in Table I are presented with roentgenograms and charts.

CASE 1.—Patient D. L. (Fig. 4), a 37-year-old white man. The patient was admitted to the hospital on the third day of lobar pneumonia of the left lower lobe (pneumococcus, Type I) and delirium tremens. Penicillin therapy was instituted immediately. On the fifth hospital day signs of pleural effusion developed and roentgenogram revealed a loculated area of fluid high in the left axilla, and a diffuse shadow over the lower one-half of left thorax. Only 30 c.c. of cloudy serous fluid was obtained by aspiration on the tenth hospital day.

The injection of SK-SD (180,000 units to 63,000 units) was followed on the next day by the aspiration of 400 c.c. of thin grossly purulent material. Up to the fifth day post-SK-SD 925 c.c. of fluid were removed, which emptied the pleural cavity of all fluid, some of which was accounted for by the local irritating effect of the enzymatic solution.

Comment: In this patient (D. L.) the immediate 24-hour clearing as seen by roentgenogram included both the upper pocketed area and lower diffuse shadow, even though the injection was given into the upper site. It seems probable that the wall of the pocket was promptly liquefied and resulted in a fusion of the total pleural area into a single compartment readily available for aspiration from a single site.

It may also be noted, in connection with earlier comments, that the fluid changed from a thin serous quality in the pretreatment to a purulent type as a result of local enzymatic action. Detailed radiographic studies have indicated that this type of change is accounted for by the release, through liquefaction, of a thick coating of exudate from the pleural surface, which floating free in the effusion appears in the aspirated material.

CASE 2.—Patient W. W. (Fig. 5), a 38-year-old Negro man. The patient was admitted to the hospital on the ninth day of an acute illness, with a massive pyopneumothorax. At least two major loculations were present. The presence of air was presumably associated with a previous thoracentesis at another hospital.

TABLE II. CASES OF BACTERIAL EMPYEMA (CULTURES POSITIVE)

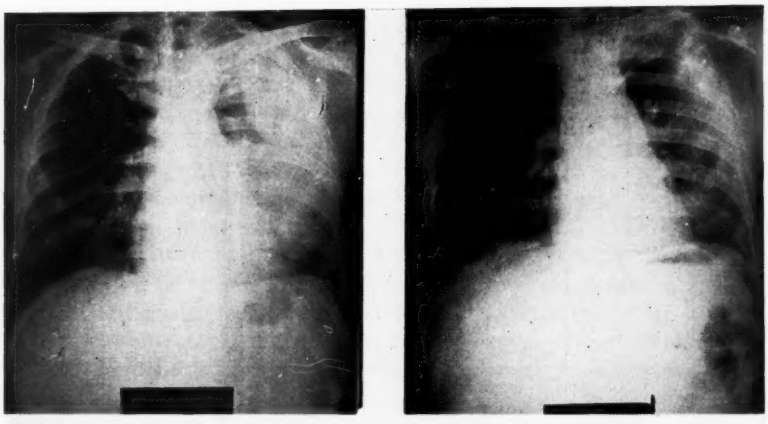
PATIENT	AGE	BACTERIOLOGY	ESTIMATED DURATION PRIOR TO SK-SD (DAYS)	EFFECT OF SK-SD ON EXUDATES		NO. INJ. SK-SD (DAYS)	BACT. CULTURES		SUBSEQUENT COURSE
				FL. JUST PRIOR TO SK-SD	FL. ASP. WITHIN 24 HOURS OF SK-SD		PRIOR TO SK-SD	WITHIN 24 HOURS POST-SK-SD	
E. B. (1)	67 (M)	Pneumo Type XXXIII	6	c.c. 100 (Cloudy)	c.c. 700 (Thin, cloudy)	3 (15)	++++	+	Recovered. See Chart 6
J. N. (2)	46 (M)	Pneumo Type XXII	?	30 (Serous)	160 (Thin, cloudy)	1	+	–	Early effect marked. Gradual, complete clearing of residual density
N. S. (3)	54 (M)	Strept. Vir.†	8	30 (Purulent)	1000 (Thin, cloudy)	2 (2)	+	–	Early effect marked. Rapid final clearing
T. L. (4)	38 (M)	Anaerobic Streptococcus	26	50 (Cloudy)	200 (Thin, cloudy, foul)	1	–(+)*	++++	Recovered. See Chart 7
W. K. (5)	68 (M)	(Mixed flora)	?	25 (Foul, purulent)	125 (Thin, non-foul)	1	+	–	Early effect marked. Gradual, complete clearing of residual density
W. P. (6)	49 (M)	*E. coli*	10	150 (Foul, purulent)	150 (Non-foul, thin)	2 (3)	+	–	Early effect marked. Gradual, complete clearing of residual density
T. F. (7)	61 (M)	*E. coli*	4	50 (Serous)	1100 (Foul, cloudy)	1	–(+)*	++	Broncho-pleural fistula was reopened. See text

All patients received penicillin or other antibiotic during period of SK-SD therapy.

*(+) signifies that earlier cultures were positive but no growth was obtained from specimen of exudate taken just prior to SK-SD.

†Strept. Vir., nonbile-soluble; possible contaminant in Type II pneumococcus pneumonia.

One injection of SK-SD (200,000 units to 50,000 units) made possible the removal of 800 c.c. and 200 c.c. of thinned fluid on two taps over a period of forty-eight hours. Roentgenograms 3*A* and 3*B* indicate the immediate 24-hour change in the empyema. Clinical improvement was also striking, but, as noted in the Chart of Fig. 4, a low grade fever persisted because of which a second injection of SK-SD was given. There was, however, no subsequent increase in the fluid obtained by aspiration. The pneumothorax disappeared within seven days following the first injection. Recovery occurred as indicated in the Chart. Ten weeks after SK-SD therapy a roentgenogram (Fig. 3*C*) indicated good expansion with some residual shadow and somewhat flattened diaphragmatic shadow, but no fluid was present.



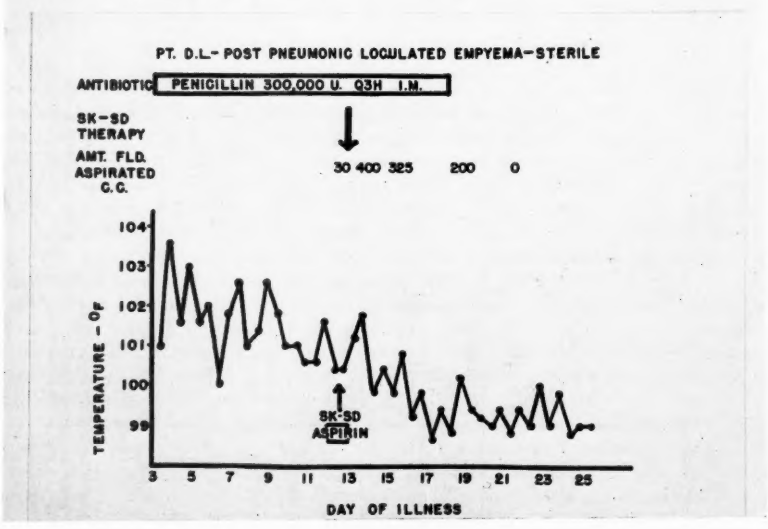


Fig. 4.—Case D. L. Loculated postpneumonic empyema, sterile. *A*. Appearance on twelfth day of illness and just prior to SK-SD therapy. *B*. Appearance twenty-four hours after SK-SD therapy and after removal of 400 c c. of purulent fluid. *C*. Graphic summary of patient's course (see text).

Comment: In the pretreatment roentgenogram it is interesting to note the bandlike shadow of the visceral pleura. It became considerably thinner within twenty-four hours after the injection of SK-SD and subsequent 24-hour aspiration, but some lateral thickening remained.

In the second group of patients (Table II) bacterial cultures of pretreatment samples of empyemal exudate were positive. They differed essentially from the group of Table I in that the infection was not controlled sufficiently

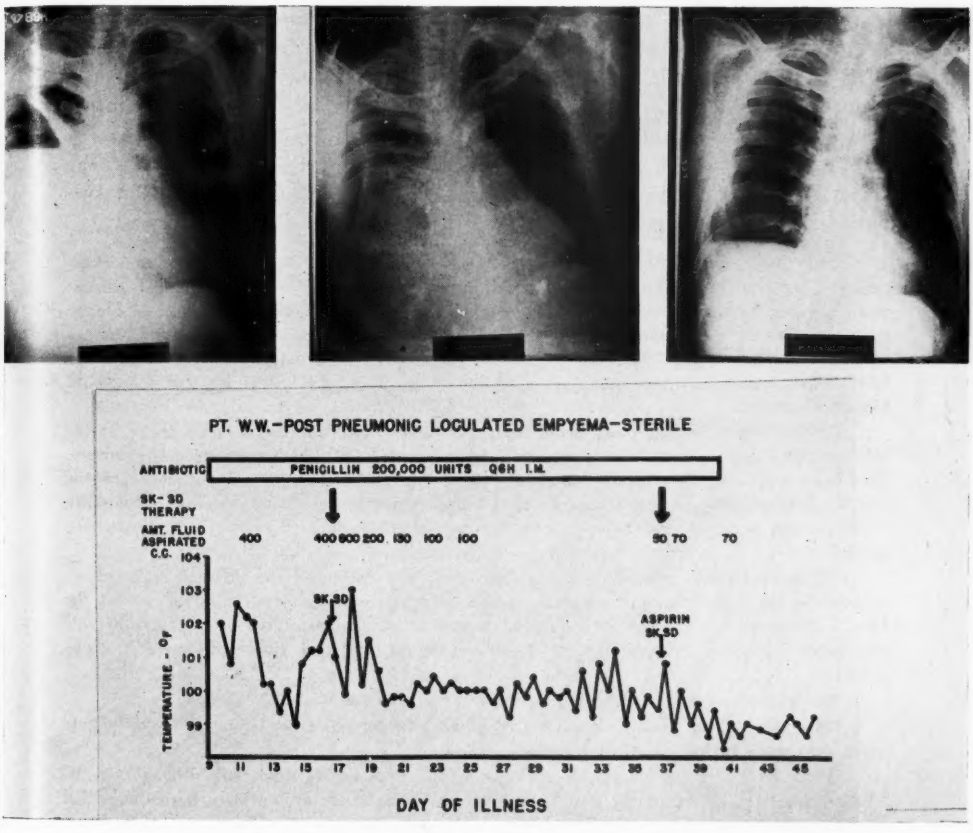


Fig. 5.—Case W. W. Loculated postpneumonic empyema, sterile. *A.* Appearance on sixteenth day of illness and just prior to SK-SD therapy. *B.* Appearance twenty-four hours after SK-SD therapy and after removal of 800 c.c. fluid. *C.* Appearance ten weeks after SK-SD therapy. The residual density continued to clear slowly spontaneously. *D.* Graphic summary of patient's course (see text).

well with antibiotic therapy to restrain the continuing multiplication of the microorganisms locally. Consequently it was possible to estimate the effect of SK-SD not only by the methods previously described, but by observing the course of the infection as measured by quantitative bacterial cultures.

It is unnecessary to comment again in detail on the data of Table II. The patients responded to the injections of SK-SD with an increase in the amount

of fluid obtained by aspiration within the first twenty-four hours which had become thinned to a low viscosity.

There was also marked improvement both clinically and radiographically following the thorough evacuation of the liquefied exudate. With the exception of patient T. F. (7), to be discussed later, the final clearing was complete.

Bacteriologically it may be noted that in four of the patients cultures that had been positive prior to the use of SK-SD became rapidly sterile. However, in the remaining two patients cultures taken just before the injections were sterile but became strongly positive immediately following enzymatic action. (The cultures on the latter two patients had originally been positive when the diagnosis of empyema was made, but had been superficially restrained by intropleural injections of antibiotics.)

In order to illustrate the relationship between the local action of the enzymes and the eradication of viable organisms the course of events in two patients is given in Figs. 6 and 7.

CASE 3.—Patient E. B. (Fig. 6) had *postpneumonic empyema* from the exudate of which pneuococcus Type XXXIII was isolated before intrapleural therapy with SK-SD. The patient was a 66-year-old white male with a history of the onset of cough, thoracic pain, and bloody sputum estimated as beginning nineteen days prior to admission to the hospital. On admission, temperature was 100.8° F. Signs of consolidation were present over the left lower lobe. White blood cells were 16,300; pneumococcus, Type XXXIII, was isolated from both blood and sputum.

On the fifth day of hospitalization the patient had developed signs of an effusion at the left base, and 1,300 c.c. of serosanguineous fluid were aspirated, which were sterile on culture. Two days later only 50 c.c. were obtained, which was also sterile. The involvement of the left side cleared. The patient then developed a hypersensitive dermatitis due to the penicillin which he had received continuously from the day of admission. Specific therapy was suspended.

During the ensuing ten days the patient gradually developed the physical signs of an effusion on the right side, and a roentgenogram revealed two areas of loculation—one at the base, and the other in the scapular region. A sample of fluid aspirated from the right side was serosanguineous, but contained flecks of coarse material and viable pneumococci, Type XXXIII.

Because of sensitivity to penicillin, sulfadiazine was administered.

The Chart in the lower part of Fig. 6 gives data derived from bacterial colony counts taken during the period of SK-SD therapy.

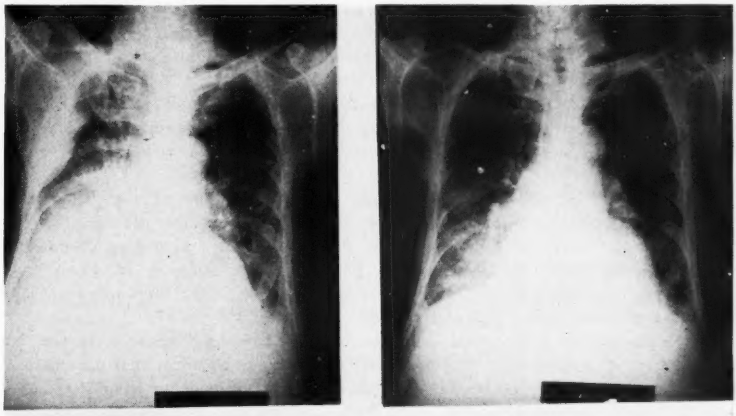
From the two roentgenograms of Fig. 6 it is interesting to note that although SK-SD (100,000 units to 20,000 units) were introduced at a single site at the base, both the pocket at the scapular area and the basal involvement cleared substantially within twenty-four hours after the removal of 700 c.c. of fluid.

From the bacteriologic chart it may be noted that the colony count of pneumococci fell during the period of two treatments with SK-SD from innumerable numbers to less than ten. The subsequent rise in the number of organisms in spite of the continuation of sulfadiazine therapy suggested the development of a fastness by the organisms in accordance with findings reported by one of us in previous studies of strains of pneumococci derived from cases of empyema.[7]

A change in therapy to aureomycin failed in three days to check the growth of pneumococci as fluid continued to reaccumulate at the base. Consequently, a third injection of SK-SD (200,000 units to 40,000 units) was administered. The precipitous drop that occurred in the colony count is apparent from the Chart of Fig. 3. Permanent recovery followed

rapidly, which may be reasonably interpreted as being due to the action of enzymatic lysis in affording effective contact between aureomycin liberated into the pleural area and the locally infecting pneumococci.

CASE 4.—Patient T. L., 38 years old, white man (Fig. 7), is one of three patients with putrid empyema who have been successfully treated without requiring surgical intervention. The patient was admitted to our Service on the twenty-fifth day of hospitalization of an acute illness that began with aspirational pneumonia followed by the development of putrid empyema.



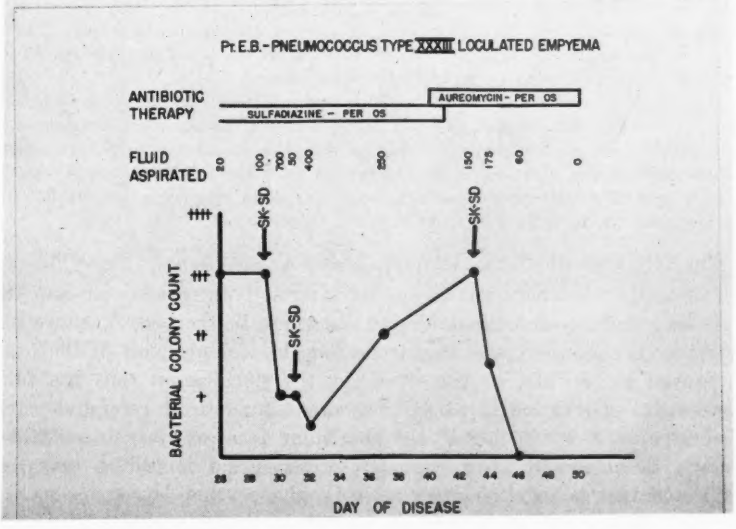


Fig. 6.—Case E. B. Loculated pneumococcal empyema. *A.* Appearance just prior to SK-SD therapy. *B.* Appearance twenty-four hours after first SK-SD injection. *C.* Graphic summary of clinical course (see text).

The legends of roentgenograms *A*, *B*, and *C* in Fig 7 serve to indicate the rapidity of the immediate change following the single injection of SK-SD and the ultimate outcome. The data in the Chart at the lower part of Fig. 7 are self-explanatory. The points of special interest may be reviewed as follows:

At the time we began to study patient T. L., cultures of the pleural exudate were sterile due to the administration of penicillin both systemically and locally. However, the febrile course and the roentgenogram indicate that a considerable degree of active disease was present.

From the Chart of Fig. 7 it may be noted that, following the injection of SK-SD (100,000 units to 20,000 units) there was a considerable increase in the amount of fluid aspirated, and also that the *cultures became positive* (++++ colony count). In addition, there was a sharp rise in fever. However, when the organisms, previously hidden within the loculations, were freed, the reinstitution of penicillin therapy given both systemically and locally resulted in the eradication of the total infection.

Putrid Empyema: Among the four patients included in Table II, who suffered from this type of suppurative pleuritis, the disease developed as a complication of aspirational pneumonia. The early samples of exudate were foul in odor and yielded positive bacterial cultures.

Three of them responded in a strikingly favorable manner through the medium of enzymatic liquefaction and appropriate antibiotic therapy. Whether or not the empyema developed by rupture of a lung abscess or by extension from suppurative pneumonitis was not determined clinically. It is interesting that the intrapulmonary infection and small pleural opening, if present, were dissipated coincidentally with the thorough evacuation and sterilization of the encapsulated pleural pockets.

The fourth patient with putrid empyema had the following course. He was operated on for carcinoma of the stomach. Postoperatively he developed aspirational pneumonia. Foul sputum in abundance was expectorated, and there was other evidence suggesting subpleural abscess. A pleural effusion developed which on aspiration was foul and purulent. A small amount of air in the pleural cavity which became evident by roentgenogram was believed to have been acquired in the process of thoracentesis rather than from a bronchopleural aperture.

On the day following the injection of SK-SD, 1,100 c.c. of foul exudate were removed. Extensive pyopneumothorax developed, with an obvious bronchopleural fistula. The fistula sealed off by the exudative coating had been reopened by the liquefying process. Thoracotomy was performed, followed by protracted chronic care.

The subject of the use of SK-SD in the presence of potential or known bronchopleural openings is of particular interest, and our experiences will be reported in a separate communication. However, as a preliminary comment it may be stated that fistulous complications have been infrequently observed in nontuberculous infections. (Note prompt clearing of three patients with putrid empyema.) The use of SK-SD in tuberculous suppurative diseases of the lungs and pleura is the subject of extensive investigation.

The Action of SK-SD in Relation to the Eradication of Bacteria.—

This subject has been one of special interest both in cases of empyema as well as in refractory infections located elsewhere in the body.[3] Since neither the streptococcal concentrates themselves nor the end products of their actions have proved bactericidal or bacteriostatic, the sterilization that has followed the successful application of SK-SD has been found to be referable primarily to the response of the tissues to the particular form of cleansing afforded by enzymatic débridement. For example, fresh serum including many of its normal constituents together with actively phagocyting leucocytes have been observed to diffuse into the areas. As a result of the liquefaction of the viscous and coarse elements of the exudates, the barrier between the humoral and cellular elements of the body just mentioned and the bacteria is removed, which

in turn has led to the destruction of the organisms. That the mechanism just described may be operative in two stages is well illustrated by the sequence of events observed in patient T. L. of Fig. 7. The application of the enzymes first uncovered viable organisms hidden in and protected by the exudate. As a result of this action the cultures became strongly positive. Following exposure

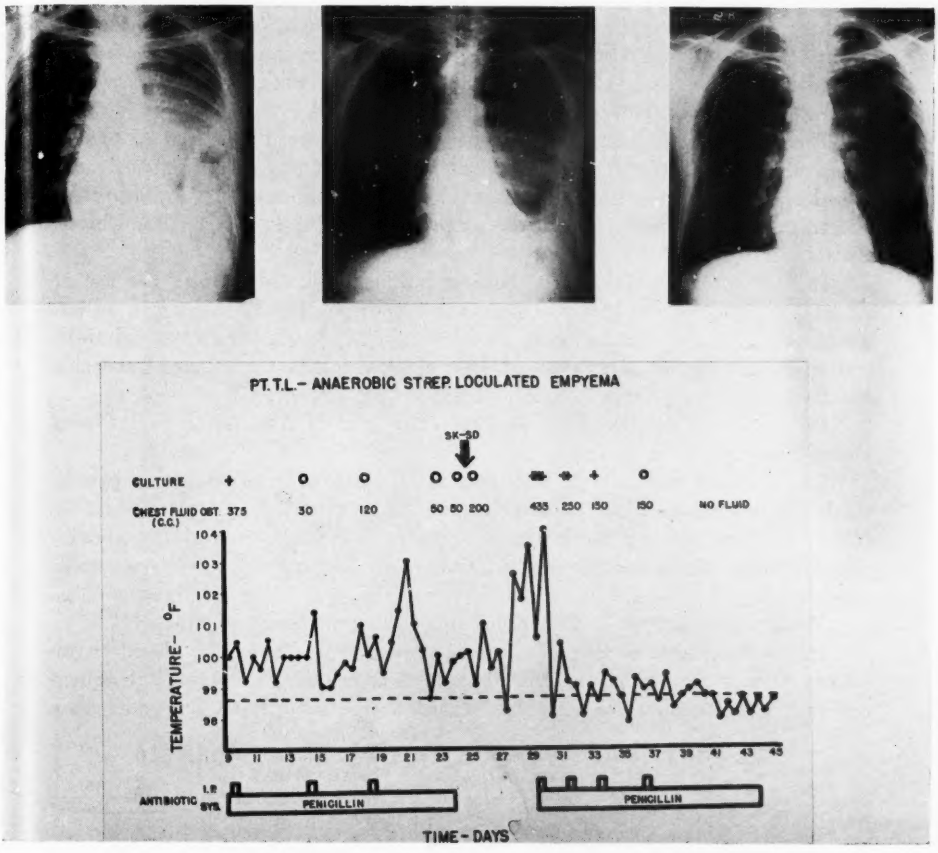


Fig. 7.—Case T. L. Loculated anaerobic streptococcal empyema. *A.* Appearance of loculated empyema at time of SK-SD therapy. *B.* Appearance twenty-four hours post-SK-SD therapy. *C.* Appearance at follow-up six months after discharge from hospital. *D.* Graphic summary of clinical course (see text.)

of the infecting streptococci, the second stage became operative during which the antibacterial elements were capable of eradicating the infection, made possible by the creation of conditions appropriate to diffusion.

Of special importance has been the increased effectiveness of antibiotic medication in the local areas subjected to enzymatic liquefaction. It has been well established that one of the problems in specific antimicrobial therapy is related to the failure to bring sufficient concentrations of penicillin and other

substances into direct contact with the organisms of the infected areas. Each of the patients with empyema of this series had received one or more of the antibiotics—before the use of SK-SD—both systemically and often intrapleurally without curative effect.

In patient T. L. of Fig. 7, even when aureomycin was finally selected for use because of the sensitivity of the infecting organism to it, its administration for three days prior to the injection of SK-SD failed to alter the local bacterial multiplication. Enzymatic instillations were, however, promptly followed by the diffusion of aureomycin into the pleural cavity under conditions which brought it into effective contact with the pneumococci.

The course of events in the two patients just described represents a principle involved in the therapeutic action of SK-SD that has been frequently observed to the effect that thick, inspissated purulent exudates can and do *protect* infecting bacteria, and that when the protective covering is abolished, antibiosis takes place rapidly.

In view of the enzymatic-antibiotic relationship just described, the use of SK-SD relatively early in acute purulent empyema is indicated when it has become evident that the character of the exudate impedes the proper administration of the forms of specific antimicrobial reagents that under favorable conditions can exert their bactericidal action.

Postpneumonic Empyemas. Medical Treatment in Association with Closed Thoracotomy.—

In exploring methods of obtaining in patients with persistent empyema, maximum re-expansion of the lung in the shortest period of time, one of us (C. T. R.) has utilized the immediate effects of SK-SD in conjunction with closed and continuous intercostal drainage in four cases of postpneumonic empyema.

Factors pertinent to the combined procedures are given in Table III.

In the treatment of two of the patients listed in Table III, closed thoracotomy was performed as the first therapeutic measure. However, subsequent drainage was unsatisfactory, and expansion of the underlying lung was poor.

TABLE III. CASES OF POST-PNEUMONIC EMPYEMA TREATED WITH SK-SD IN ASSOCIATION WITH CLOSED THORACOTOMY

PATIENT	AGE (SEX)	ESTIMATED DURATION PRIOR TO TREATMENT	TIME RELATION OF INJECTION OF SK-SD TO OPERATION*	NUMBER OF INJECTIONS SK-SD (DAYS)	DURATION OF TUBAL DRAINAGE (DAYS)	SUBSEQUENT COURSE
E. M. (1)	57 (M)	17	1. Operation 2. SK-SD	3 (4)	7	See Fig. 8
E. G. (2)	35 (M)	25	1. Operation 2. SK-SD	2 (4)	6	Final clearing complete
C. W. (3)	56 (M)	6	1. SK-SD 2. Operation 3. SK-SD	2 (2) 2 (2)	8	Final clearing complete
R. C. (4)	34 (M)	30	1. SK-SD 2. Operation 3. SK-SD	2 (2) 1	7	Final clearing complete

*In the first two patients of the Table, thoracotomy preceded the use of SK-SD. In the third and fourth patients SK-SD was injected first followed by thoracotomy, which in turn was followed by instillations of SK-SD. (See text.)

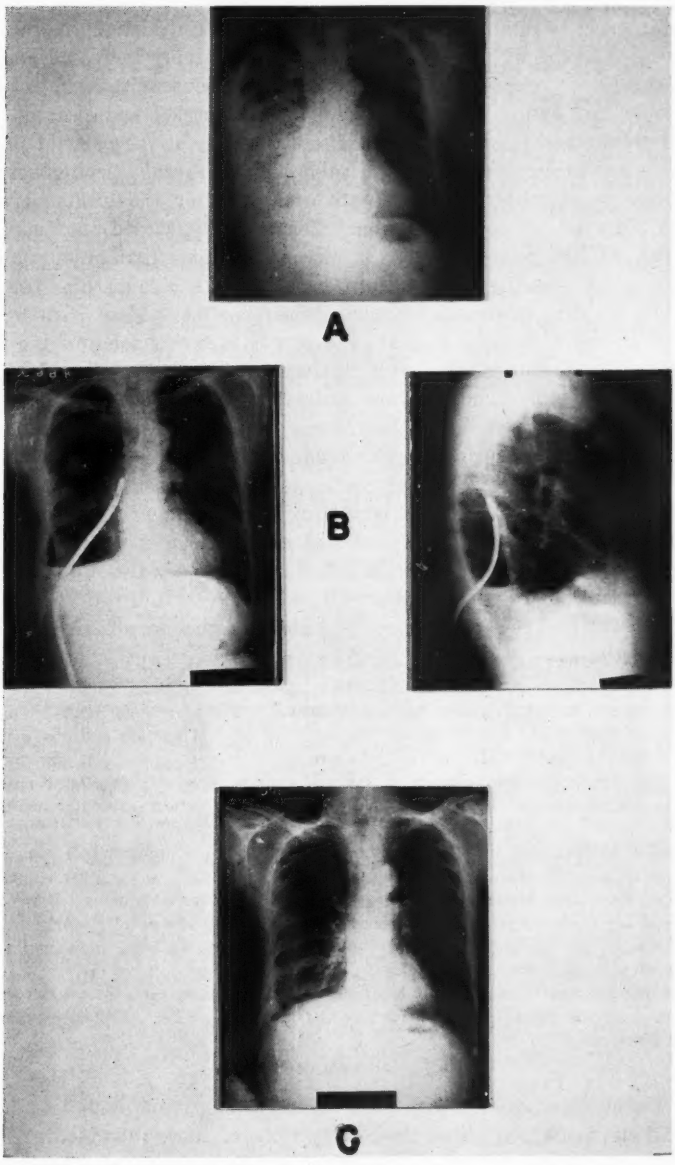


Fig. 8.—Case E. M. Loculated postpneumonic empyema, sterile. *A.* Appearance just prior to thoracotomy and SK-SD therapy. *B.* Appearance in (1) posteroanterior and (2) lateral after closed thoracotomy to show size of empyema space. *C.* Appearance seven days later, following two SK-SD injections and removal of tube. (Empyema space is almost completely obliterated.)

Consequently, SK-SD was introduced through the drainage tube which was then clamped in order to retain the solution, in situ. When drainage was reinstituted by opening the tube six to eight hours later, considerably increased amounts of thinned fluid were released. Repetitions of instillations were given as indicated in the table, and within seven days the empyemal pocket had cleared, the tube was withdrawn, and the lung expanded to the border of the parietal pleura.

In the remaining two patients of Table III, the initial injections of SK-SD, given prior to operation, did not satisfactorily alter the loculated areas or densities observed by roentgenogram. Consequently, closed thoracotomy was performed. When postoperatively it was still obvious that evacuation of the exudate was not occuring rapidly, solutions of SK-SD were instilled through the tube as in the first two cases. Clearing then became evident both by the increased drainage of thinned exudate and extensive reexpansion of the underlying lungs. The drainage tubes were removed within the ensuing eight days.

It should be pointed out that the patients just described were, on admission to the hospital, seriously ill with bacteremic pneumococcal pneumonia on which empyema was subsequently superimposed. When the bacteremia and other aspects of invasiveness were brought under control with penicillin, the effort was made to handle the local purulent complication by utilizing the advantages that might be derived from both surgical and enzymatic measures. This type of study is being extended in order to define more exactly the optimal means in the total treatment of empyema that will hasten most rapidly the eradication of active infection and the restoration of maximum pulmonary expansion.

CASE 5.—Patient E. M., 57-year-old white man (Fig. 8), is illustrative of the results that have been obtained in four cases treated in this manner.

The patient, in delirium tremens, was admitted in a serious condition with lobar pneumonia of the right lower lobe, duration unknown. Blood and sputum cultures were positive for pneumococcus, Type VII. Under intensive therapy with penicillin, aureomycin, and streptomycin, his temperature decreased, but a loculated empyema developed on the right side. In spite of repeated aspirations (cultures sterile) an extensive roentgenogram shadow persisted.

On the fourth week after admission, a closed thoracotomy was performed, and by thoroscopy the empyemal cavity was visualized. It conformed to the outline of the right lower lobe. The pleural surfaces were coated with a yellowish amorphous jellylike coagulum with interlacing fibrinous strands. A microscopic pathologic report of material obtained by biopsy described the specimen as being granulation tissue with an acute inflammatory reaction and covered with fibrinopurulent exudate.

The patient was treated with SK-SD through the tube on three occasions over a four-day period. By the eighth postoperative day the lung was almost completely expanded, and the tube was removed.

SUMMARY

1. Twenty-one patients with postpneumonic empyema, including four cases of putrid empyema, have been treated with one or more intrapleural injections of streptococcal concentrates containing streptokinase and streptodornase (SK-SD). In eighteen of them, including three cases of the putrid type, the liquefying action of the enzymes was followed by improvement that ranged from rapid termination of the disease by crisis to marked immediate improvement followed by subsequent progressive defervescence.

In the successfully treated patients the prime objective of the lytic enzymatic therapy was accomplished by making possible within twenty-four hours the extensive evacuation of the loculated encapsulated empyemal cavities followed by significant increases in the re-expansion of the underlying lung.

In addition, when active infection was demonstrable by positive bacterial cultures, the enzymatic débridement was followed by rapid sterilization of the local area frequently in association with specific antibiotic therapy. The mechanism of the action of SK-SD in relation to the eradication of local infections has been discussed.

2. In two patients with postpneumonic empyema treated on the thirtieth and forty-second day of disease, the enzymatic injections were not significantly effective, presumably because of the extent to which cellular organization had taken place. In one of the patients with putrid empyema, liquefaction with SK-SD was followed by the extensive reopening of a bronchopleural fistula that made subsequent treatment more difficult.

3. In four patients with postpneumonic empyema, injections of SK-SD were employed in association with closed thoracotomy. The results were highly favorable in evacuating the exudate and promoting reexpansion of the lung.

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MONOSTOTIC FIBROUS DYSPLASIA OF BONE

Report of a Case Involving Three Contiguous Ribs Treated by Wide Resection of the Thoracic Cage

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THE solitary cystic bone lesion proves of interest to the clinician, roentgenologist, pathologist, endocrinologist, and surgeon. The problem presented revolves about the classification of the lesion, and each member of the diagnostic team encounters equal difficulty in making a correct evaluation. Considerable progress has been made in the pathologic classification of solitary bone cysts. Fibrous dysplasia has been confused with osteitis fibrosa cystica, giant-cell tumors, Albright's syndrome, chondroma, eosinophilic granuloma, solitary bone cysts, solitary chloroma, osteoid osteoma, ossifying fibroma, fibrosarcoma, Paget's disease, metastatic new growth, and neurofibroma of bone. Intercostal nerve tumors, aneurysm, cold abscess, encapsulated empyema, and bronchogenic carcinoma have in some instances resembled primary rib tumors.

We are reporting a case of monostotic fibrous dysplasia which developed in the right fourth rib and involved the third and fifth ribs. The case is of interest because it demonstrates the locally invasive behavior of this tumor, the large size the tumor may attain, the difficulties of correct diagnosis, and the satisfactory convalescence and rehabilitation of a patient who was submitted to an extensive resection of the thoracic cage.

HISTORIC REVIEW

Hedblom[1] in 1933 reported a review of 313 tumors of the bony chest wall, 261 of which were tumors of the ribs. Sommer and Major[2] in 1942 reviewed eighty-one additional cases including fifteen cases from the University of Michigan Hospital. They reported no five-year cures for malignant tumors and only two cases of osteogenic sarcoma with a three-year survival. Dorner and Marcy,[3] in 1948, reviewed twenty-two additional cases, including seven from the Iowa University Hospital. These writers are all in agreement that wide excision is the treatment of choice for primary tumors of the rib and sternum. Results were universally poor in malignant tumors. These reviews placed no particular emphasis on a class of tumors which are now recognized as solitary bone cysts due to a benign fibrous dysplasia of bone.

Lichtenstein and Jaffe,[4] in 1942, reviewed ninety cases of fibrous dysplasia of bone including fifteen of their own. Fifteen cases had lesions limited to one bone, thirty-two (35.0 per cent) were associated with skin pigmentation.

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Schlumberger,[7] in 1946, reviewed sixty-seven cases of fibrous dysplasia of single bones studied at the Army Institute of Pathology, of which twenty-nine (43.0 per cent) occurred in the rib. None of these cases exhibited skin pigmentation or endocrine dysfunction. All were young service men, and 45.0 per cent of the rib lesions were first diagnosed and suspected on routine chest roentgenography.

ETIOLOGY AND INCIDENCE

Fibrous dysplasia of bone has been considered to be the result of multiple factors, namely: first, developmental defect resembling a hamartoma (Lichtenstein and Jaffe);[4] second, neurologic defect (Albright);[5] third, excessive estrogen circulation (Bremer);[6] fourth, disturbed reparative process following bone trauma (Schlumberger);[7] and fifth, a manifestation of neurofibromatosis (Tannhauser).[8] The definite establishment of the causative factors may ultimately substantiate the existence of multiple causes for the pathologic pictures that are recognized. Lichtenstein and Jaffe reported fifty-one female and thirty-five male patients in their collected series. Although the disease usually appears at an early age, an age range from 5 to 61 years is reported. Schlumberger reports a distribution of lesions as follows: ribs, twenty-nine; femur, nine; tibia, eight; maxilla, seven; calvarium, five; mandible, two; and vertebra, one. These were all single lesions. Lichtenstein and Jaffe reported fifteen single lesions, seventeen multiple but limited lesions, twenty-nine with lesion restricted to one side, twenty-six with generalized extensive lesions and 35.0 per cent with cutaneous pigmentation.

Pathologic studies have endeavored to place polystotic fibrous dysplasia, Albright's syndrome, and monostotic fibrous dysplasia in a common classification. The presence of endocrine dysfunction in certain lesions, variability of distribution of lesions, wide age distribution, factor of trauma, and presence of associated developmental anomalies necessarily make it difficult to explain all manifestations upon a common etiologic basis. Until such time as additional information can be secured, theoretical speculation and conjecture must suffice.

CLINICAL MANIFESTATIONS AND DIAGNOSIS

Lesions of fibrous dysplasia become manifest clinically as follows: first, localized swelling associated with local tenderness and discomfort; second, spontaneous pathologic fracture; third, routine roentgenography of the chest; fourth, unusual cutaneous pigmentation developing on the head, neck, buttocks, and extremities; and fifth, precocious puberty in girls. The diagnosis is suspected from the roentgenogram appearance of the lesion. The lesion usually appears as an irregular rarefaction of bone abutting on one or more cortices causing thinning and possible expansion of the cortex, but rarely producing a perforation. Surrounding the area of rarefaction there may be a narrow zone of increased density. Bony trabeculae may traverse the rarefied area giving a lobulated picture. Lesions do not cross the epiphyseal plate. A pathologic fracture is not uncommonly seen.

The diagnosis is made in the long bones by biopsy, and treatment is carried out according to the pathologist's findings. Inasmuch as a solitary lesion may be metastatic, all the possible primary lesions should be investigated preoperatively. Serum calcium, phosphorus, and acid and alkaline phosphatase determinations are within normal limits in fibrous dysplasia, but may be altered in Paget's disease, metastatic lesions, and osteitis fibrosa cystica.

GROSS AND MICROSCOPIC PATHOLOGIC LESIONS

The lesion may be a fusiform expansile type causing an expansion of the cortex, but not breaking through the cortex. Other lesions show a normal bony contour, but exhibit an atrophy of the cortex. The periosteum strips with ease. Cross section shows a tissue of a rubbery and often gritty type ranging from a white to a white-yellow color. Cystic degenerative areas are frequent. Bony trabeculae are common. The basic cellular structure is a monotonous connective tissue composed of small, slender, spindle cells. Collagen is present inversely proportional to the cellularity. Myxomatous areas are occasionally observed. Nests of small giant cells having less than twelve nuclei are scattered throughout the connective tissue. New bone tissue is laid down by plump spindle cells in a rather disorganized pattern. Microscopically, the lesions can be differentiated from a giant cell tumor whose cells contain a large number of nuclei. Fibrous dysplasia tissue, microscopically, is indistinguishable from that of a solitary bone cyst or osteitis fibrosa cystica.

TREATMENT

The proper treatment for solitary lesions of the rib is wide excision of the lesion removing pleura, intercostal nerve, and thoracic muscle en masse as necessary to effect a complete removal of the tumor. Cutting into the tumor mass to make a frozen section diagnosis is not recommended because of the danger of spillage of malignant cells. It is preferable to remove the lesion in a manner that would be selected were it a known malignant lesion. The results reported with the use of radiation therapy indicate minimal curative benefits.

Reconstruction of the thoracic cage may be accomplished by a variety of techniques. The defect may be closed by using split segments of ribs to effect a bony stabilization of the chest wall, as reported by Maurer and Blades.[9] Watson and James[10] made use of fascia lata graft in large defects. Maier[11] devised a plastic procedure utilizing the opposite breast. Pickrell, Kelley, and Marzoni[12] devised a variety of pedicled flaps to be used in closing the defect. Campbell[13] made use of a fascia lata graft, transplantation of the latissimus dorsi muscle, and covering this with a split thickness skin graft to effect a closure of a three-rib defect.

CASE REPORT

The patient was a 41-year-old white man admitted to Lima Memorial Hospital Oct. 22, 1947. He complained of a painful tumor of the right chest wall situated in the region of the anterior axillary fold. The tumor had been enlarging for the past seven months.

In March, 1947, the patient experienced a sudden spontaneous excruciating pain anterior to the right axillary fold as he abducted his arm. The patient became so distressed he was unable to continue at work. Swelling occurred during the next twenty-four hours in the area noted. The pain and swelling persisted, and a roentgenogram of the chest was made approximately five weeks after the onset of the initial acute pain. A large tumor involved the right fourth rib, and the patient was advised to have surgical intervention. During the following six months the mass gradually enlarged filling the right axilla. The patient experienced a gradual weight loss of twenty pounds, persistent mild discomfort over the tumor mass, and a moderate dyspnea upon exertion. There was no history of chronic cough, hemoptysis, or pleuritic pain. No symptoms were experienced referable to the head, neck, gastrointestinal, or genitourinary organs.

The patient's father had died at the age of 66 years from myocarditis. His mother was living and enjoying satisfactory health at the age of 72 years. There were two brothers, aged 47 years and 38 years, both living and well. There were twin sisters, aged 36 years, living and well. The patient gave a history of having had no previous illnesses other than scarlet fever, mumps, measles, and streptococcic lymphangitis in the left leg at the age of 18 years.

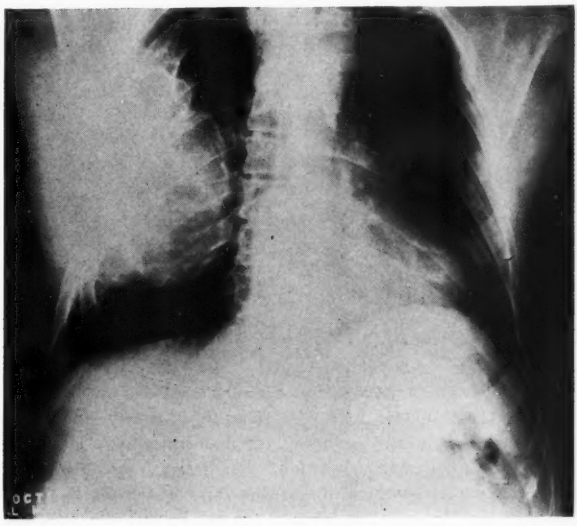

Fig. 1.—Roentgenogram of thorax showing an expanding trabeculated lesion of the right chest.

Physical examination revealed a man sixty-four inches (162.56 centimeters) in height and weighing 142 pounds (64.4 kg.). The blood pressure was 120/72. Pulse rate was 88, the temperature 98.6° F., and the rate of respiration 18. Physical examination revealed no abnormalities except for that portion of the examination pertaining to the thoracic cage. There was a large expanding, hard, fixed, tender tumor mass filling the right axilla between the midaxillary and midclavicular planes. Anteriorly, the third, fourth, and fifth ribs were palpated as they appeared to enter the tumor mass. Examination of the urine for albumin, sugar, bacteria, and microscopic cellular elements gave negative results. The test for Bence-Jones protein was negative. The concentration of hemoglobin was 15.1 Gm. per 100 cubic centimeters of blood; there were 5,210,000 erythrocytes, and 7,900 leucocytes per cubic millimeter of blood. There were 26 per cent lymphocytes, 68 per cent mature, and 6 per cent band forms of polymorphonuclear leucocytes on the differential

count. The Kline test gave a negative result. Determinations of the blood urea nitrogen was 15 mg. per 100 c.c. of blood, and of the total serum protein 5.56 Gm. per 100 cubic centimeters. The Cutler blood sedimentation rate was recorded to be 16 mm. in one hour. Posterior-anterior, lateral, and oblique roentgenograms of the chest showed a tumor of the right chest confined to the third, fourth, and fifth ribs. The roentgenogram appearance of the tumor revealed an outer capsule or shell. The tumor measured 14 cm. by 13.5 cm. through its widest diameters, enclosing what appeared to be a multiloculated cyst. A preoperative diagnosis of a primary cystic tumor of the right fourth rib with invasion of the third and fifth ribs was made. A malignant tumor was suspected. On Oct. 30, 1947, Dr. Roger L. Tecklenberg administered an endotracheal anesthetic consisting of sodium pentothal, nitrous oxide, oxygen, and ether. The patient was placed in the left lateral position, and an incision was started medial to the scapula, curved inferiorly around the angle of the scapula, and carried anteriorly over the fourth rib. The pectoralis major,

Fig. 2.—Photograph of surgical specimen showing the pleural surface.

latissimus dorsi, trapezius, serratus anterior, and rhomboidalis muscles were divided and the scapula was elevated. A large tumor was found involving three-fourths of the fourth rib and two-thirds of the third and fifth ribs. The third, fourth, and fifth ribs containing the tumor were removed en masse beginning the mobilization by a disarticulation of the fourth rib at the sternocartilagenous junction. The entire fourth rib and three-fourths of the third and fifth ribs were resected, disarticulating the fourth rib posteriorly from the costovertebral junction. The superior lobe of the right lung was adherent to the pleura overlying the tumor mass involving an area two centimeters by eight centimeters. The adhesions were easily separated as the tumor had not penetrated into the lung tissue. We appeared to be well beyond the tumor at all points in our resection of the chest wall. Three hundred thousand units of penicillin were placed in the pleural cavity. Four small strips of Gelfoam were placed in the costovertebral area. The muscles of the chest wall were approximated with interrupted chromic catgut No. 1 sutures. The skin was closed with No. 000 silk. The operating time was two and one-half hours.

Dr. Frederick A. Hemsath reported on the pathologic specimen as follows:

"*Gross Examination:* The specimen consists of a large, hard, bony tumor which is intimately attached to several ribs. The total weight is 1,000 grams. Total length of the excised ribs is 28 cm. The tumor presents a glistening, slightly bossed surface projecting into the thoracic cavity. It measures 15 by 9 by 9.5 cm. The peripheral border of the mass extends along the course of the ribs as a flattened mass. On transverse section of the

midportion the ribs are considerably distorted and their structure is lost. On cross section the mass shows a considerable amount of cortical calcification, and central portions appear firm, gray to brown in structure.

"*Microscopic Examination:* Sections of the decalcified material show a layer of cortical bone along the surface. The balance of the structure is replaced by a tumor composed of spindle cells which shows a myxomatous structure in a few small areas. For the most part they are arranged as interlacing bundles, and in many areas bone is laid down directly without the presence of cartilage. Certain areas show a considerable number of giant cells with centrally placed groups of nuclei. Nuclei of the tumor are fairly uniform in size and structure. The microscopic picture is that of fibrous dysplasia of bone."

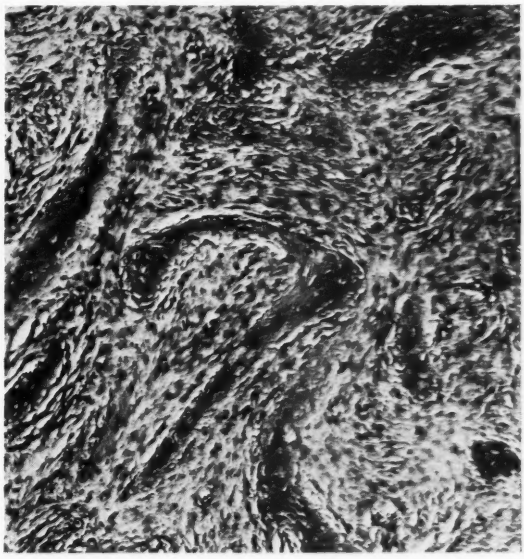

Fig. 3.—Photomicrograph of tumor.

The patient was given a transfusion of 1,500 c.c. of whole blood during the twenty-four hours postoperatively. A mucous plug of the right main bronchus was aspirated by means of a tracheal catheter twenty-four hours postoperatively. A thoracentesis on Nov. 1, 1947, removed 275 c.c. of serosanguineous fluid. Thoracentesis repeated on Nov. 7, 1947, removed 200 c.c. of serous fluid. The patient was given 50,000 units of crystalline penicillin every three hours. The convalescence was uneventful, and the patient was dismissed home on the twelfth postoperative day, at which time the wound was well healed. A chest roentgenogram revealed only a slight amount of pleural thickening in the right base. The patient's general condition was satisfactory. There was a tendency toward herniation of the thoracic muscles covering the anterolateral chest wall defect. This was controlled by use of a tight dressing. The patient has been followed nearly three years since surgery, and there is no evidence of a local recurrence of the tumor. Subsequent chest roentgenograms have remained entirely normal. The patient has been working full time at his occupation and has experienced no unusual symptoms. He continues to have a moderate herniation of the chest wall when he coughs or sneezes; otherwise, he has experienced no discomfort or respiratory embarrassment from the loss of the bony structure of the right thoracic cage.

COMMENT

The involvement of three ribs suggested the preoperative diagnosis of a malignant tumor. There was no evidence of a primary tumor, and surgical extirpation of the large tumor was indicated. A technique as described was utilized making a wide excision of the mass. Closure of the thoracic cage defect was accomplished posteriorly by the scapula. Anterolaterally, the preserved pectoralis major muscles and the remnant of the serratus anterior gave a satisfactory closure. This allowed a huge parietal pleural defect to remain from which there developed a moderate amount of serosanguineous effusion which was easily controlled. The patient's only inconvenience has been a slight anterolateral thoracic herniation during episodes of coughing and sneezing. He has noted no dyspnea nor interference with his usual activities. The pathologic diagnosis favored by Dr. Frederick A. Hemsath initially was a low-grade osteogenic sarcoma, primary in the rib. After considerable study, he concluded the lesion was that of monostotic fibrous dysplasia. Dr. Hans Schlumberger later reviewed the sections and concurred in the pathologic diagnosis.

The patient has now been well for nearly three years which speaks against malignancy. The destruction of the ribs may have resulted from a pathologic fracture sustained by the patient in March. At that time he noted a sudden severe pain in the region which became enlarged in the next twelve hours and subsequently did not disappear, but continued to enlarge. Evidently, there was an extravasation of blood and fibrous dysplasia tissue about the site of the fracture and, as weeks passed, this tissue produced a destruction of the rib above and below the original lesion with replacement by the fibrous dysplasia tissue. This particular tumor may prove the connecting link between benign fibrous dysplasia and those few cases that have terminated in a full-blown sarcoma. Grossly, the tumor had the typical characteristics of a locally invasive malignancy destroying all normal tissue and still presenting a smooth encapsulated periphery.

SUMMARY

An unusual case of monostotic fibrous dysplasia involving the right third, fourth, and fifth ribs presenting local malignant invasive features has been reported.

The surgical procedure and three-year follow-up have been presented.

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HETEROTOPIC GASTRIC MUCOSA IN THE ESOPHAGUS WITH ULCERATION AND STRICTURE FORMATION

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HETEROTOPIC gastric mucosa may occur in almost any portion of the gastrointestinal tract. Complications resulting from aberrant gastric mucosa are best known to the clinician in connection with Meckel's diverticulum where peptic ulceration leads to hemorrhage or to diverticulitis with or without perforation. In the esophagus heterotopic gastric mucosa occurs most frequently in the postcricoid region. In this location Schridde[1] found aberrant islets of gastric mucosa in 70 per cent of autopsied cases. The islets vary in size from microscopic dimensions to 1 or 2 centimeters in diameter. Such islets may occasionally be recognized endoscopically as shallow depressions of pinkish epithelium. In a study based on single, random microscopic sections Rector and Connerley[2] found among 1,000 consecutive autopsies in children eighty-nine cases of heterotopic gastric mucosa in the esophagus. In only twenty-six of the eighty-nine cases were parietal cells found in the mucosa.

The presence of gastric mucosa in the esophagus assumes clinical importance in connection with peptic ulceration and adenocarcinoma. Chronic peptic ulceration of the esophagus occurs in the lower third of this organ, and is not infrequently associated with stricture formation. The etiology of this condition is still debated, but Allison[3] presents convincing evidence for the following pathogenesis in most instances: a sliding hernia of the stomach initiates the process by permitting regurgitation of acid contents into the esophagus. Esophagitis, ulceration, and fibrous healing follow with stenosis and shortening of the esophagus as secondary phenomena. However, several authors[4, 5, 6] have reported finding peptic ulcerations in the lower third of the esophagus in association with heterotopic gastric mucosa. Despite the more frequent occurrence of gastric mucosa in the upper fourth of the esophagus, we are not aware of any such complication in that region.

We have recently encountered a unique case of heterotopia in which the lower half of the esophagus was completely lined with gastric mucosa. At the junction between gastric and squamous epithelium, at a level in the esophagus with the aortic arch, ulceration and stricture formation had occurred (Figs. 1 and 2). One should distinguish carefully between this anomalous condition and thoracic stomach associated with short esophagus. In our case a small, easily reducible hiatal hernia was noted by barium study, but at operation the entire stomach lay below the diaphragm. The lower half of the esophagus was resected and the stomach then elevated to the apex of the chest.

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CASE REPORT

A 63-year-old white woman was admitted to the Chest Surgical Service of Barnes Hospital on Jan. 23, 1950. The patient had first noted occasional difficulty in swallowing fifteen years previously. Her main symptoms at that time, however, consisted of postprandial epigastric fullness, nausea, eructations, and sour stomach. Four years before admission her dysphagia increased. During the six months prior to admission her symptoms progressed until finally her diet was reduced to liquids. From time to time she experienced a small hematemesis while eating. Food seemed to stick in the midchest region. Tincture of belladonna afforded little relief. She had lost 20 pounds during the latter part of her illness.

Fig. 1.—Esophagram revealing high stricture. Small hiatal hernia is visible just above diaphragm.

In October, 1949, she had been admitted to another hospital. Barium studies showed normal gastric motility. There was a small hiatal hernia which was easily reducible. Examination of the esophagus revealed an area of fusiform narrowing at the arch of the aorta (Figs. 1 and 2). The mucosal markings were intact, and the stricture appeared benign. At esophagoscopy an annular narrowing was encountered 23 cm. from the incisor teeth. The mucosa was red and bled easily. A 5 mm. esophagoscope was passed through the stricture, and the latter appeared to extend several centimeters along the esophagus. Nothing was stated concerning the character of the mucosa at or below the stricture. A

biopsy taken from the lesion showed inflammatory cells only. The patient's symptoms failed to improve following this instrumentation. She was admitted to Barnes Hospital three months later.

Physical examination showed an obese female weighing 183 pounds with a hypertension of 190-110. Otherwise the physical examination was not remarkable. The routine laboratory examinations were within normal limits. A barium study of the esophagus revealed essentially the same findings as previously recorded.

Fig. 2.—Esophagram in oblique position showing high stricture formation. Smooth narrowing suggests benign lesion and associated spasm.

Esophagoscopy was repeated, and revealed a rather marked narrowing at the level previously mentioned. The mucosa appeared somewhat redundant, granular, and bled easily. A biopsy taken from the lesion showed gastric mucosa. Because of inability to rule out carcinoma, and because of the advanced nature of the stricture, an exploratory thoracotomy was performed. The left fifth and eighth ribs were resected subperiosteally. An optimum exposure was obtained by working alternately through these two regions. Palpation above and below the arch demonstrated no tumor mass, but suggested some thickening of the esophageal wall. The stomach lay entirely below the diaphragm. After mobilization of the stomach transection was made through the cardia, and the esophagus reflected superiorly. An esophagogastric anastomosis was started about 1 cm. above the aortic arch. However, the esophagus at the line of division showed thickened mucosa and ulceration. A frozen section from this area demonstrated the presence of gastric mucosa. Accordingly, the posterior line of the anastomosis was taken down and a second resection performed more proximally through normal esophageal mucosa close to the apex

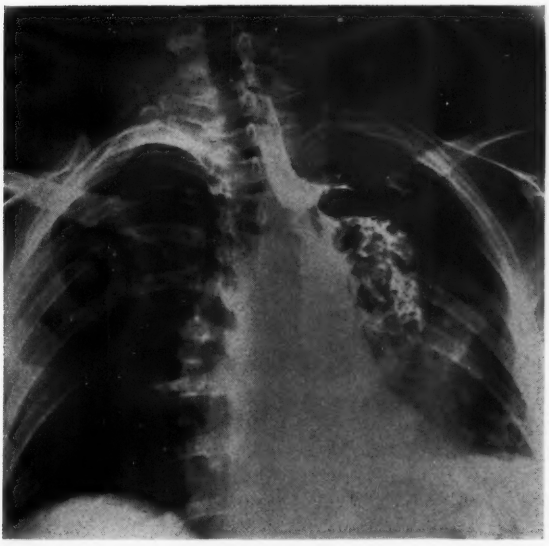

Fig. 3.—Esophagram showing esophagogastric anastomosis and high position of stomach.

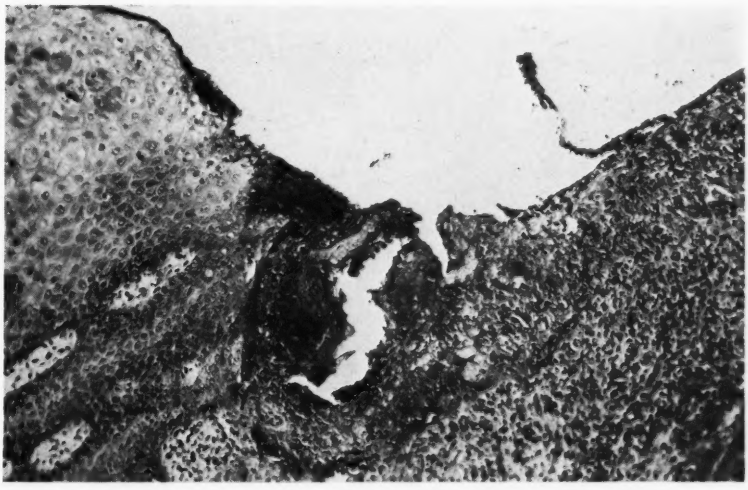

Fig. 4.—Photomicrograph showing section at upper end of resected esophagus. The stratified squamous epithelium has been partially replaced by a chronic ulcer. (×135.)

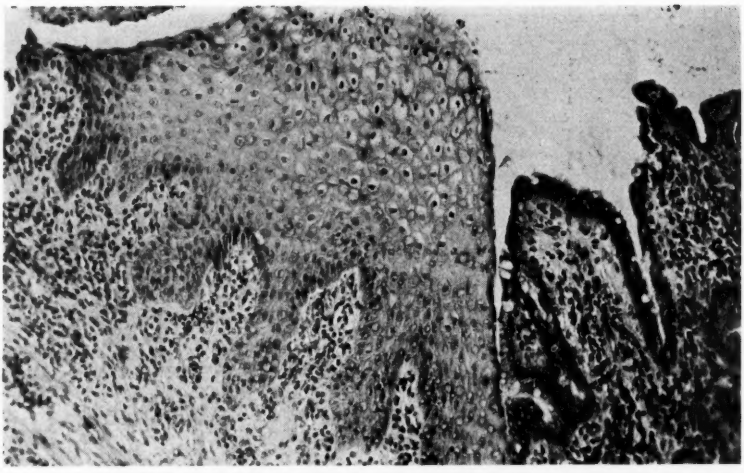

Fig. 5.—Photomicrograph showing section at transition between squamous and gastric epithelium near upper end of specimen. (×140.)

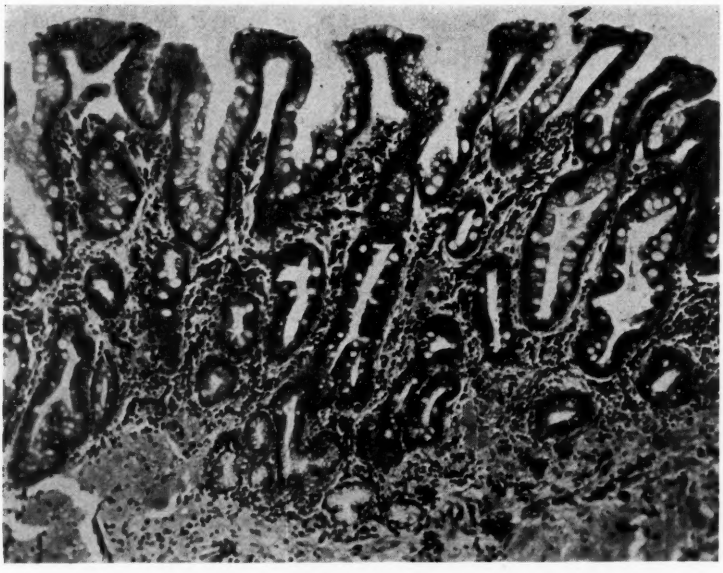

Fig. 6.—Photomicrograph showing heterotopic gastric mucosa with diffuse infiltration with lymphocytes. (×135.)

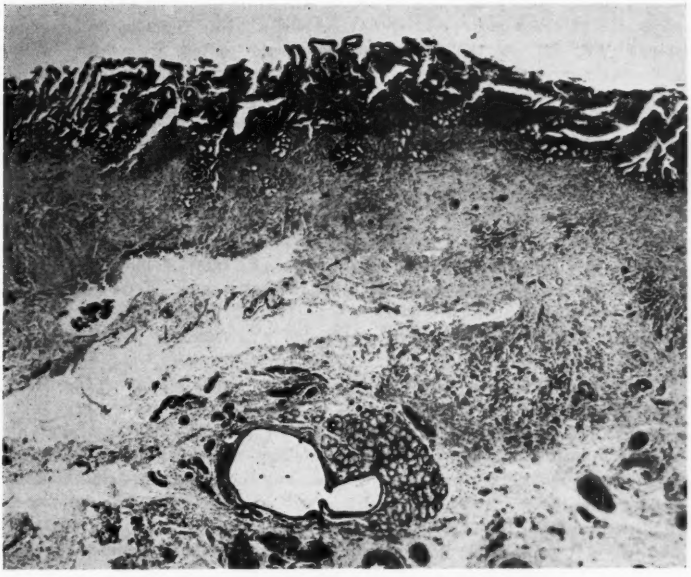

Fig. 7.—Photomicrograph showing low power view of middle portion of resected esophagus. A cluster of esophageal glands lies deep in the submucosa beneath gastric type epithelium.

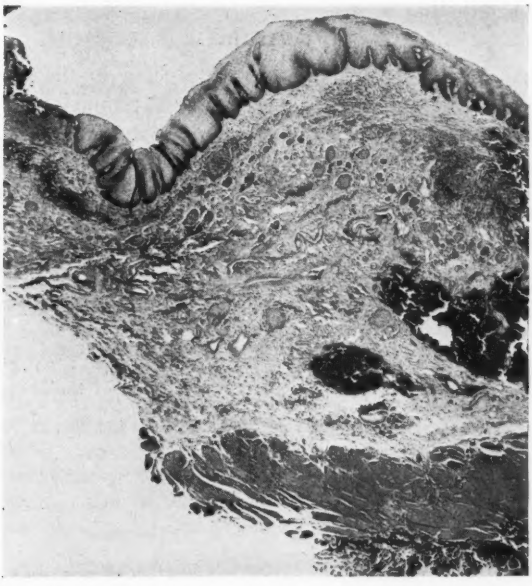

Fig. 8.—Photomicrograph showing low power view of upper end of resected esophagus at the point of stricture. The submucosa is markedly thickened and fibrosed.

of the pleural space. The postoperative course was quite satisfactory. A barium swallow performed on the fifteenth postoperative day showed a freely functioning anastomosis with a wide lumen (Fig. 3). At the time of discharge the patient was eating well but complaining of some regurgitation.

Gross Description.—(Specimen No. 50-535). The resected segment of esophagus, after marked retraction, measured 10 cm. in length. A 0.5 cm. segment of stomach was continuous with the lower end of the esophagus. The esophageal mucosa was thickened and granular throughout. At the proximal end of the esophagus the mucosa was replaced by several superficial ulcerations, measuring 0.5 to 1 cm. in diameter, some of which were coated by a white exudate. The submucosa was thickened and fibrotic, especially at the proximal end of the esophagus where the lumen was moderately constricted. An additional segment of esophagus measuring 2 cm. in length was resected from the remaining intact esophagus by the surgeon in order to remove completely the zone of ulceration and stricture. Where present, the mucosa of this segment was somewhat thickened.

Microscopic Description.—The entire specimen was cut into blocks which were sectioned at various levels.

The 2 cm. cuff of proximal esophagus removed separately was lined with thickened stratified squamous epithelium. In some areas the mucosa was replaced by a shallow ulceration the floor of which consisted of connective tissue and inflammatory cells (Fig. 4). A sharp transition existed between squamous epithelium and gastric mucosa (Fig. 5). The entire surface of the larger esophageal specimen was lined with gastric mucosa composed of glands which contained goblet cells, but no parietal cells. Lymphocytes were scattered throughout the gastric mucosa (Fig. 6). Superficial erosion of the epithelium was noted at several points. A cluster of esophageal glands lay deep in the submucosa beneath the gastric glands (Fig. 7). At the site of stricture the submucosa showed marked thickening with fibrosis (Fig. 8). The ulceration and associated fibrosis described involved predominantly the esophagus just proximal to the junction of squamous and gastric mucosa. The microscopic diagnosis was heterotopic gastric mucosa with ulceration, esophagitis, and stricture formation.

SUMMARY

An unusual case of heterotopic gastric mucosa in the esophagus is presented. The lower half of the esophagus was lined completely with gastric type mucosa. At the transition between squamous and gastric mucosa chronic ulceration and stricture had occurred. This anomalous condition must be differentiated from thoracic stomach and short esophagus associated with stricture formation.

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ANOMALOUS LOBE OF LUNG ARISING FROM THE ESOPHAGUS

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AN ANOMALOUS lobe of lung arising from the esophagus is a rare congenital deformity. In view of the common embryologic origin of the esophagus and the respiratory system, it is surprising that no report of such a deformity, and only a few cases resembling this deformity have appeared in medical literature.

CASE REPORT

History.—S. K., a 5-month-old female infant, weighing 12 pounds, 3 ounces, was admitted to the Children's Memorial Hospital on Nov. 3, 1949, with a history of chronic cough, pallor, rapid respiration, intermittent fever, and failure to gain weight. At birth, following an uneventful pregnancy, the infant was seemingly healthy and weighed 10 pounds, 7 ounces. Fever and rapid respiration were noted on the third day of life. Roentgenograms of the chest at the age of one month revealed what appeared to be atelectasis of the left upper lobe. Bronchoscopic examination done elsewhere showed no abnormality at that time. Esophagoscopy was not done. Coughing was always the outstanding symptom, and was frequently associated with vomiting. Solid foods were not tolerated. Since the age of 2 months the child had three severe upper respiratory infections, and from then until the time of admission had been given 100,000 to 200,000 units of penicillin daily. During five months she had gained one and one-half pounds in weight.

Physical examination revealed a pale, irritable, puny child. Respirations were 40 per minute, the pulse was 120, and the temperature was 100.6° F. Positive physical findings were limited to the chest—dullness and absent breath sounds over the left upper chest anteriorly and posteriorly.

The hemoglobin was 6.6 Gm., the red blood count was 2,970,000, and the white blood cell count was 20,300. The differential count was normal. Urine examinations were negative.

Multiple translucent areas were seen in the region of the left upper lobe in roentgenograms of the chest (Fig. 1).

Bronchoscopic and esophagoscopic examinations were made by Dr. Paul Holinger. Bronchoscopy revealed a left lower lobe bronchus somewhat compressed posteriorly with little air exchange in the left lower lobe. The left upper lobe bronchus was likewise compressed and had no air exchange whatsoever (Fig. 2). A flexible curved aspirator could be advanced only a few millimeters into this bronchus. During esophagoscopy a large amount of thick, yellow-green pus was aspirated. At about the level of the bifurcation of the trachea a fistula or diverticulum almost as large as the esophagus itself could be seen (Fig. 3), and appeared to be lined with normal mucous membrane. With each respiration pus was expelled freely from this fistula into the lumen of the esophagus.

The patient was given three blood transfusions, penicillin, and streptomycin. An episode of high fever and rapid respirations up to 60 per minute occurred while on this treatment, but subsided when aureomycin was added. The red blood cell count was brought up to 4,930,000, and the hemoglobin to 10.8 Gm.

Operation.—On November 17, under intratracheal oxygen-ether-cyclopropane anesthesia, the chest was opened by a posterolateral incision through the left fourth interspace. A soft, smooth mass about 8 cm. in diameter was found in the apex of the left chest. It was covered with a smooth movable membrane which when opened proved to be the pos-

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terior parital pleura. While dissecting the mass from its bed considerable foul smelling pus was expressed into the esophagus and aspirated. The left main bronchus was firmly adherent to the inferior margin of the mass but did not communicate with it. The blood supply consisted of two fairly large arteries arising from the left pulmonary artery. After these were cut the mass was free except for the large fistula to the esophagus. This communication was doubly occluded with nontraumatic ductus clamps and cut. The stump on the esophagus was closed with a double row of fine interrupted No. 00000 silk sutures. The retropleural space was lavaged with 1 to 1000 zephiran solution and drained with a catheter inserted through the third interspace posteriorly. The parietal pleura was closed over the drain. The compressed upper lobe was expanded readily by pressure on the anesthetic bag. The general chest cavity was drained by a de Pezzer catheter inserted from the inside out through the fifth interspace. The chest wall was closed in layers with surgical gut and the skin was closed with silk.

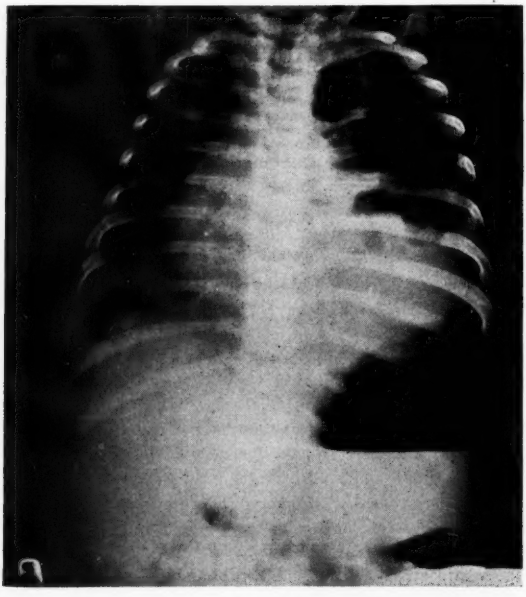

Fig. 1.—The upper half of the left lung appears to be cystic. The lower half is partially atelectatic.

The postoperative course was uneventful. The pleural cavity drain was removed on the second day, and the retropleural drain was removed on the sixth day. The patient was discharged on the twelfth day after operation. Since then recovery has been rapid and weight gain above average.

Pathology.—The gross specimen was covered with a thick fibrous capsule. Entering one side of the mass was a firm tubular structure 10 mm. in circumference, 15 mm. long, and containing islands of cartilage (Fig. 4). As it entered the mass it bifurcated into two channels which in turn broke up and were lost in the substance of the tissue. The cut surfaces revealed many cystlike cavities 8 to 10 mm. in diameter, containing air, pus, and necrotic tissue.

Microscopic examination of the tubular structure confirmed the presence of islands of cartilage and revealed a lining of pseudostratified, columnar epithelium. The tunica propria

Fig. 2.—Lipiodol outline of the bronchial tree indicates that the left bronchus is being pushed downward.

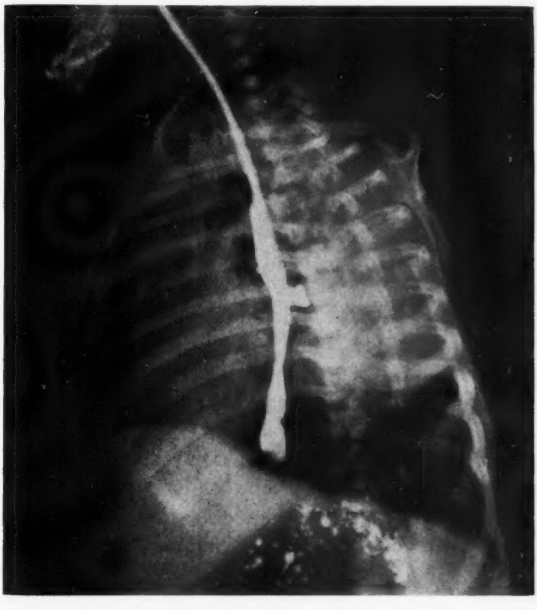

Fig. 3.—Esophagram outlines the fistula from the esophagus. Lipiodol did not enter the anomalous lobe.

was composed of collagenous and elastic fibers with marked round-cell infiltration. Smooth muscle fibers were seen, and typical glands such as are normally found in the trachea were present in the submucosa. The mass itself consisted of atelectatic lung parenchyma and bronchioles filled with myriads of polymorphonuclear cells, necrotic material, and occasional vegetable cells. Pathologic diagnosis was ectopic bronchus and lung originating from the esophagus and chronic aspiration pneumonia.

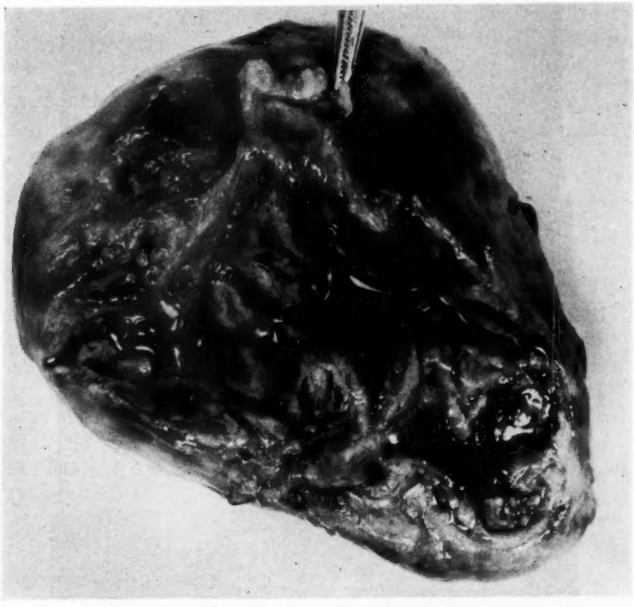

Fig. 4.—Gross specimen. The hemostat is attached to the opened bronchuslike tract.

EMBRYOLOGY

In early fetal life the esophagus and trachea are one structure. The beginning of the respiratory system is an outpouching from the foregut just caudal to the pharyngeal pouches. Outside of the gut this is known as the laryngotracheal ridge. The upper end of the ridge advances cephalad and forms the laryngeal structures. The lower end of the ridge becomes split off from the gut and forms the trachea and lung bud. The lung bud bifurcates, forming two lung buds which ultimately produce all the subdivisions of the respiratory tree. On the right side two lateral buds appear; the upper forms the apical or or eparterial bronchus, and the other is the stem for the middle lobe. The original right stem bud forms the lower lobe. On the left side a single lateral bud appears which later forms the upper lobe while the stem bud forms the lower lobe. The left upper lobe appears to have another bronchial branch which is equivalent to the right apical or eparterial lobe, but it remains small and rarely forms a separate lobe. During this same period the lumen of the esophagus becomes filled with rapidly proliferating cells. Vacuoles appear in the epithelial masses and they coalesce to form the normal lumen of the esophagus.

These primordia of the different parts of the respiratory system and esophagus develop within a mass of mesenchyme which later becomes the mediastinum. The original right and left bronchial buds carry an investment of this mesenchyme as they grow laterally into their future pleural cavities. This mesenchyme differentiates later into the muscle, connective tissue, and cartilage of the bronchi and their branches, and into it grow blood vessels and nerve fibers.[1, 2]

DISCUSSION

On the basis of the above embryological background, it is not difficult to explain most of the congenital anomalies which take place in this region. The origin of tracheoesophageal fistula is obviously an incomplete separation of the laryngotracheal groove from the gut.[3] Such a fistula may be an opening between an otherwise normal trachea and esophagus, or it may coexist with an atresia of the esophagus.

Another group of related abnormalities appear to arise from the early gut as independent evaginations of tissues with respiratory potentialities. Mohr[4] has reviewed five cases by other authors and presented three cases of his own in which cysts of the esophageal wall were found which were lined with the ciliated columnar epithelium of the respiratory tract. Another such case was reported in the Case Records of the Massachusetts General Hospital in 1947.[5] Scheidegger[6] described a case of a premature infant who had an anomalous lobe of lung adherent to the pleural side of the left leaf of the diaphragm. It did not communicate with the respiratory system but was connected to the stomach by a tract lined with gastric mucosa. Morton, Osborne, and Klassen[7] reported a case of a 26-year-old man with bronchiectasis caused by a broncho-esophageal communication which was lined with intestinal tract mucosa. In this case an independent evagination from the foregut presumably attached itself to and made a communication with an otherwise normal bronchus. In our case and in that of Scheidegger, it is not unreasonable to postulate that a group of cells representing the anlage of a lung lobe was somehow mislocated in the wall of the early gut and proceeded to evaginate and develop in a manner similar to that of a normal lobe but retaining its embryonic connection with the gastrointestinal tract. One might further suppose, in our case, that the anomalous lobe should have been the left eparterial segment or lobe since it received all its blood supply from the pulmonary artery.

SUMMARY

1. We have presented a case in which an anomalous lobe of lung communicating with the esophagus by means of a bronchuslike tract was found in the chest and successfully treated surgically.

2. The embryology of the origin of the esophagus and respiratory system from the gut is briefly reviewed.

3. The origin of this and similar anomalies is discussed.

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A REPORT OF TWO CASES OF THE ANOMALOUS ORIGIN OF THE RIGHT SUBCLAVIAN ARTERY FROM THE DESCENDING AORTA

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THE aberrant origin of the right subclavian artery from the descending aorta is not uncommon, and on roentgenogram studies of the esophagus it is being recognized with increasing frequency.[1, 2] Dysphagia due to pressure of this vessel on the posterior surface of the esophagus is the usual complaint, though even this symptom is rarely present. On physical examination there are no signs to indicate the presence of this aberrant vessel when there are no associated anomalies. Two cases were observed recently at Duke Hospital, and are recorded because one had the unusual symptom of tracheobronchial obstruction without dysphagia. In the other case the aberrant artery was not the cause of symptoms, but because of an associated coarctation of the aorta presented unusual physical signs.

The description of the origin and explanation of the development of an aberrant right subclavian artery has been reviewed in several recent articles.[2, 3, 4] The vessel arises from the posterior medial surface of the first part of the descending aorta and courses posterior to the esophagus in nearly all cases, though in some instances it may pass between the esophagus and trachea, or even anterior to the trachea.

The diagnosis by roentgenogram examination of the esophagus is not difficult, and has been well described in the recent literature.[2, 3]

CASE REPORTS

Case 1.—(C-70963) A 19-year-old white man was admitted to Duke Hospital because a routine employment examination had revealed hypertension. The patient denied any symptoms referable to the cardiovascular system or gastrointestinal tract.

On examination the blood pressure by cuff measurement was found to be 210/95 in the left arm, 110/80 in the right arm, and 135/0 in the right and left legs. Pulsations were palpable but feeble in the right arm and both lower extremities. Strong pulsations were noted in both carotid arteries. The heart was enlarged to the left with a Grade I systolic murmur over the aortic area. There were palpable arterial pulsations in the chest wall.

The accessory clinical findings showed the hemoglobin to be 15.1 Gm., white blood cells, 9,450, with a normal differential. The urine showed a faint trace of protein but normal microscopic findings.

The roentgenogram of the chest showed an enlarged heart, small aortic knob on the left side, and notching of the ribs. On barium swallow the esophagus was found to be slightly indented on its left side by the aortic knob with a more pronounced indentation on the right just above this area, while its posterior surface was indented in an oblique manner beginning in the region of the arch. The electrocardiogram was within normal limits.

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On Feb. 6, 1949, a left thoracotomy was carried out. In the aorta, a typical adult type of coarctation was found in a left descending aorta with a large branch arising from the posterior surface of the first portion of descending aorta just below the stricture (Fig. 1). On constriction of this vessel the pulsations in the right radial artery increased, and the blood pressure in this extremity rose from systolic 120 to systolic 160. This vessel was ligated and divided. The aorta in the region of the stricture was resected and an end-to-end anastomosis was carried out.

CASE 2.—(C-72590) Since birth this 18-month-old white girl had been having respiratory infections characterized by wheezing respirations, cough, dyspnea, and temperature elevation. These recurred every two to four months and persisted for one to two weeks. The last episode began two weeks before admission to Duke Hospital.

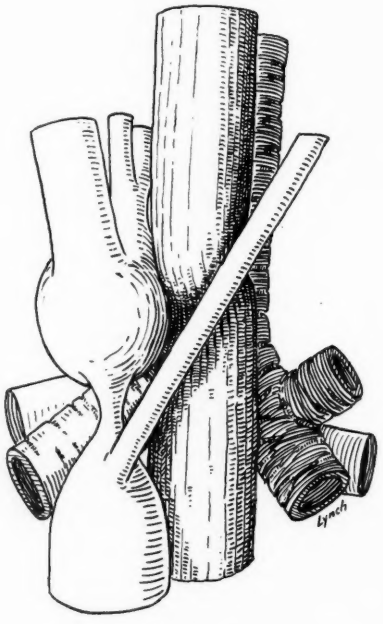

Fig. 1.—Drawing showing the relation of the aberrant right subclavian artery to the stenosed aorta and the esophagus in Case 1.

On examination, the patient's temperature was 40° C. She was a well-developed and well-nourished acutely ill white child. Respirations were labored and accompanied by cough and moderate inspiratory supraclavicular retraction. There were numerous râles in both lungs. Breath sounds were less distinct on the right than on the left.

The hemoglobin was 12 Gm., the white blood count 12,000, and the urine normal.

Roentgenogram examination of the chest showed the lung on the right to be more radiolucent than the left, with a homogeneous density in the superior aspect of the right chest (Fig. 2). The left lung was normal. The trachea and mediastinum were shifted to the left. On fluoroscopy there was mediastinal shift to the right on inspiration and to the left on expiration. Bronchograms showed obstruction and displacement to the left of the trachea more pronounced in the lower one-third. The left bronchial tree was well filled.

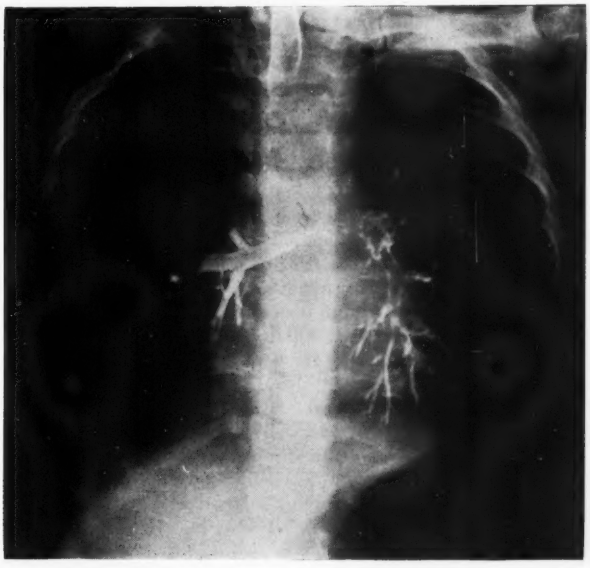

Fig. 2.—Bronchogram showing displacement of the lower trachea to the left with distortion of the right stem bronchus. The trachea can be seen filled in its upper one third.

Fig. 3.—Barium-filled esophagus in Case 2 showing the displacement of the esophagus to the right (*A*) and suggestive area of constriction high on the posterior esophagus above the normal aorta constriction (*B*).

The right stem bronchus was pulled upward and angulated sharply, and displaced toward the left. The upper and middle lobe bronchi did not fill. On barium swallow there was angulation of the upper esophagus, which was shifted to the right with a long pressure defect on its left border beginning in the middle one-third; while on its posterior surface there was a slight indentation (Fig. 3).

Bronchoscopy showed almost complete obstruction of the trachea in the lower one-third.

Immediately after admission to the hospital the patient developed difficult wheezing respirations, and temperature elevation necessitating oxygen and treatment with penicillin and streptomycin. After ten days this improved, but was followed in five days by another similar episode. Eight weeks after admission to the hospital under ether anesthesia an exploratory mediastinotomy through a midline sternal splitting incision was carried out avoiding both pleural cavities. At operation an aberrant right subclavian artery was found arising from a left descending aorta just where the ligamentum arteriosum was attached. This arose posteriorly beyond the origin of the left subclavian artery, and coursed behind the trachea and esophagus. There was a palpable narrowing of the lower one-third of the trachea, while the esophagus was deviated to the right. The subclavian artery did not seem to impinge upon the trachea, but had pulled the descending aorta over to the right posterior to the trachea. This allowed the trachea and origin of the right stem bronchus to be caught between the ascending and descending aorta. On division of the right subclavian artery between ligatures the two ends of the artery separated very widely allowing the descending aorta to retract to the left.

A the end of the operation the patient's temperature was 41.8° C. In spite of vigorous attempts to lower the temperature, the patient had a generalized convulsion five hours after operation and died.

Postmortem examination failed to reveal any cause for the sudden death. The aortic arch was found to be in the normal position with the right carotid and left carotid arteries arising from the transverse aorta adjacent to each other. The left subclavian artery arose in its normal position, while the right subclavian artery originated from the first part of the descending aorta posteriorly and at the level of the ligamentum arteriosum.

DISCUSSION

The first case was typical of coarctation of the arota except for the normal blood pressure in the right arm and elevated blood pressure in the left arm. In view of the normal position of the aorta, the discrepancy in blood pressure recording could be explained only by the origin of the right subclavian artery below the stricture. This was confirmed by finding typical pressure defects in the esophagus on barium swallow.

In the second case, the preoperative diagnosis was an anomaly of the aorta, though its exact configuration was not appreciated. The wide displacement of the esophagus to the right in the presence of a normal left arch seemed to rule out either a double arch or a right arch. The absence of dysphagia with clinical and x-ray indications of right bronchial obstruction appeared to be against the diagnosis of a right subclavian artery originating from the left descending aorta. At operation the origin of the right subclavian artery was easily exposed through the midline because of the marked deviation of the descending aorta to the right from the pull on it from the aberrant artery. The right subclavian artery was posterior to the esophagus and was not exerting any significant pressure either on the esophagus or trachea. The esophagus was displaced to the right by proximity of both the ascending and descending aorta. The right

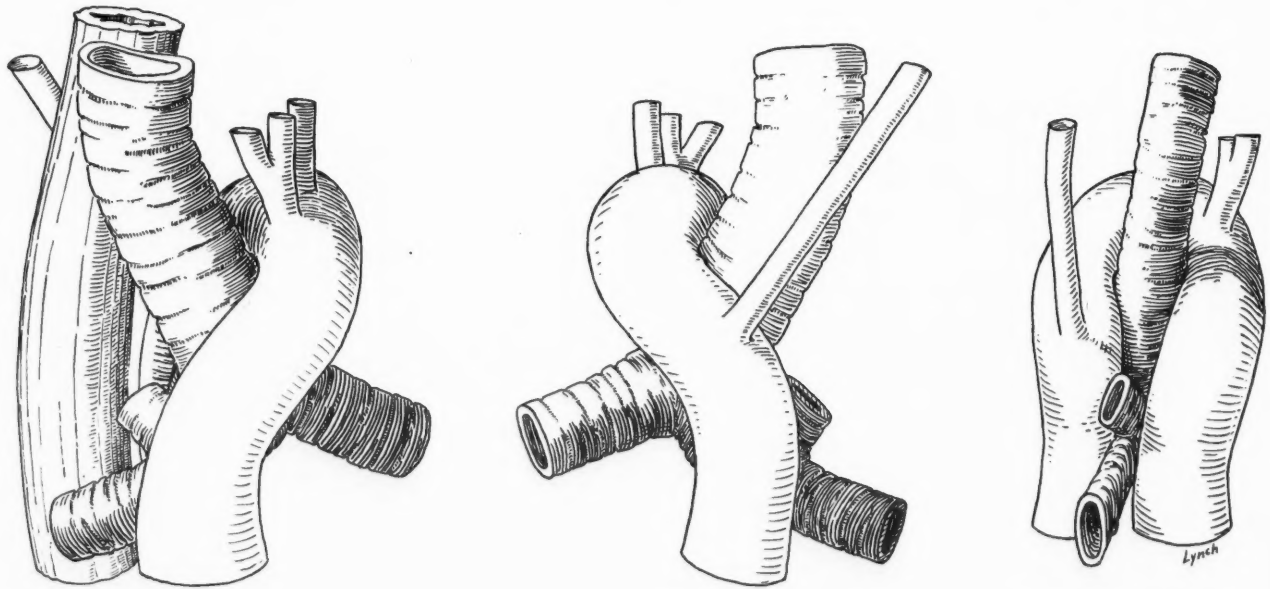

Fig. 4.—Drawing of the displacement of the descending aorta by the aberrant right subclavian artery in Case 2 demonstrating the mechanism of tracheal and right bronchial compression. The esophagus is omitted from the posterior and lateral projections.

bronchus and lower trachea were caught and almost completely obstructed by the viselike cleft consisting of the ascending aorta in front and the displaced descending aorta posteriorly.

In retrospect, the diagnosis in Case 2 would be suggested by the following points: (1) partial tracheal and right bronchial occlusion without esophageal obstruction, (2) displacement of the esophagus to the right and the trachea to the left, and (3) a left aortic arch.

CONCLUSION

Two cases with an aberrant right subclavian artery originating from the descending aorta are reported. In one case there was an associated coaretation of the aorta giving rise to diminished pulsations and blood pressure in the right arm. The second case was unusual in that the aberrant subclavian artery caused displacement of the descending aorta in such a way that right bronchial and lower tracheal obstruction occurred without esophageal obstruction.

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